REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	November 1999	Unknown

4. TITLE AND SUBTITLE
An evaluation of the effectiveness of 75 mcg/kg of preservative free morphine and 1.5% mepivacaine with 1:200,000 epinephrine into the brachial plexus sheath of patients receiving surgery to the hand, forearm, proxial arm, or shoulder in...

5. FUNDING NUMBERS

6. AUTHOR(S)
MAJ Debra Clise
CPT Craig Budinich
CPT Timothy Huffman
CPT Laure Kline
CPT Lesa Rathjen

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Unknown

8. PERFORMING ORGANIZATION REPORT NUMBER
HSC-SN-99-xxxxxxx

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Unknown

10. SPONSORING / MONITORING AGENCY REPORT NUMBER
NA-1999-02

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; Distribution is unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*
Missing Abstract.

14. SUBJECT TERMS
Anesthesia, Brachical Plexus, Postoperative Pain, Surgery, Hand, Arm, Shoulder

15. NUMBER OF PAGES
138

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
UNCLASSIFIED	UNCLASSIFIED	UNCLASSIFIED	UL

AN EVALUATION OF THE EFFECTIVENESS OF 75 MCG/KG OF PRESERVATIVE FREE MORPHINE AND 1.5% MEPIVACAINE WITH 1:200,000 EPINEPHRINE INTO THE BRACHIAL PLEXUS SHEATH OF PATIENTS RECEIVING SURGERY TO THE HAND, FOREARM, PROXIMAL ARM, OR SHOULDER IN AFFECTING THE ONSET OF POSTOPERATIVE PAIN WHEN COMPARED TO 1.5% MEPIVACAINE WITH 1:200,000 EPINEPHRINE.

By

MAJ Debra Clise, B.S.N., CPT Craig Budinich, B.S.N.,

CPT Timothy Huffman, B.S.N., CPT Laure Kline, B.S.N.,

CPT Lesa Rathjen, B.S.N

A Thesis

submitted in partial fulfillment

of the requirements for the degree of

Master of Science in Nursing

The University of Texas Health Science Center at Houston

School of Nursing

November 1999

THE UNIVERSITY OF TEXAS
HEALTH SCIENCE CENTER AT HOUSTON
SCHOOL OF NURSING

REPORT OF THESIS EXAMINING COMMITTEE

STUDENT'S NAME: Student ID#
MAJ Debra Clise
CPT Craig Budinich
CPT Scott Huffman
CPT Laure Kline
CPT Lesa Rathjen

THESIS TITLE: Will the preoperative injection of 75 mcg/kg of preservative free morphine and 1.5% mepivacaine with 1:200,000 epinephrine into the brachial plexus sheath of patients receiving surgery to the hand, forearm, proximal arm, or shoulder affect the onset of postoperative pain when compared to 1.5% mepivacaine with 1:200,000 epinephrine?

DATE REVIEWED: 12 October 1999

DECISION OF THE COMMITTEE

The student has been examined by the Committee with the following results:

X **Approved** _____ **Rejected**

SIGNATURES OF EXAMINING COMMITTEE MEMBERS

1. Eileen A Hegmann — Chairperson — Date: 8 NOV 99
2. Katherine A. Hamilton — Member — Date: 8 NOV 99
3. Cynthia Griffith — Member — Date: 8 NOV 99
4. Joseph A Bulas — Member — Date: 8 NOV 99

_____ _____
Associate Dean for Academic Affairs Date

THE DEAN OF THE SCHOOL OF NURSING ACCEPTS THE COMMITTEE'S DECISION

_____ _____
Dean's Signature Date

_____ _____
Title of Degree Graduation Date

TABLE OF CONTENTS

Page

Page

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

Introduction

Brachial plexus anesthesia is an effective anesthetic technique used to provide reliable anesthesia for a variety of surgical procedures performed on the hand, forearm, proximal arm, and shoulder. In several clinical trials, investigators demonstrated that the success rates of the most frequently used approaches (axillary, interscalene, supraclavicular, and infraclavicular) ranged from 70% to 100% (Urmey, 1996). Each of these approaches has distinct advantages and disadvantages when compared to general anesthesia and to each other. In addition, the duration of anesthesia is dependent on the duration of action of the local anesthetics injected into the brachial plexus sheath. Methods aimed at improving postoperative analgesia provided by brachial plexus anesthesia offer the possibility of improved postoperative analgesia with decreased frequency of side effects and complications. One method is the addition of an opioid to the local anesthetic solution to delay the onset of postoperative surgical pain (Bourke & Furman, 1993).

In order to provide postoperative analgesia, opioids are frequently administered intravenously, intramuscularly, epidurally, and intrathecally. Side effects are associated with these routes of administration. According to Ransom and Leicht (1996), the side effects associated with the epidural administration of morphine sulfate for postoperative analgesia in 1,000 cesarean section patients included pruritus (46% of patients) and nausea and vomiting (20% of patients). In addition to the side effects associated with the epidural administration of opioids, Reisine and Pasternak (1996) described the potential

for respiratory depression, convulsions, and chest wall rigidity following the intravenous and/or intramuscular administration of opioids.

In several animal and human studies, investigators have demonstrated that functional opioid receptors are not only present in the central nervous system, but also are found in the peripheral nervous system (Lan, Wen, Tan, Ling, & Shieh 1995; Stein, Millan, Shippenberg, Peter, & Herz 1988). These findings provide a foundation for further research. The focus of this research was to explore the effects of adding an opioid to a standardized local anesthetic solution for brachial plexus anesthesia.

The addition of an opioid to a brachial plexus local anesthetic solution provides extended postoperative pain relief while minimizing the systemic adverse effects of intravenous and/or intramuscularly administered opioids (Bazin et al., 1997). The most common adverse effects reported by Bazin et al. (1997) following the administration of morphine, buprenorphine, or sufentanil in combination with bupivacaine and epinephrine in 80 patients receiving brachial plexus anesthesia were drowsiness, pruritus, nausea, and vomiting. The most severe adverse effect observed was vomiting, while respiratory depression was not seen (Bazin et al., 1997).

Several researchers have examined the effects of combining an opioid with a standardized local anesthetic solution administered into the brachial plexus. The results were equivocal. Racz, Gunning, Della Santa, and Forster (1991) conducted a clinical investigation ($n = 50$) in which it was demonstrated that the addition of 5 mg of morphine to a 1% lidocaine and 0.5% bupivacaine solution for axillary brachial plexus anesthesia did not provide significantly longer postoperative analgesia than that provided by 5 mg of morphine administered intramuscularly together with a 1% lidocaine and 0.5%

bupivacaine solution deposited into the brachial plexus sheath. A probability value of less than 0.05 was considered significant by the authors, but no specific level of significance was provided. On the other hand, Bourke and Furman (1993) found that the addition of 0.1 mg/kg of morphine to a 1.5% lidocaine solution with 1:200,000 epinephrine to the brachial plexus sheaths of subjects who underwent surgery of the upper extremity consumed fewer analgesic capsules than subjects who received the local anesthetic solution alone ($p < 0.05$). The control group consumed an average of two more analgesic capsules (Mdn = 4; range = 0 - 12) than the experimental group in the 24 hour period following surgery (Mdn = 2; range = 0 - 7).

Brachial plexus anesthesia offers many benefits to both the patient and the health care system. Urban and Urquhart (1994) noted that, in contrast to general anesthesia, brachial plexus anesthesia eliminated the requirement for endotracheal intubation and provided postoperative analgesia when local anesthetics and opioids were used. Brachial plexus and other regional anesthetic approaches allowed for the early discharge of patients from outpatient surgical units and decreased the amount of postoperative analgesics administered (Kehlet & Dahl, 1993). Kehlet and Dahl also stated that adequate treatment of postoperative pain may expedite recovery and restore function, resulting in a reduction of postoperative morbidity and hospital stay. If the addition of an opioid to the brachial plexus anesthetic solution can delay the onset of postoperative pain beyond the effective duration of action of the local anesthetic with minimal adverse side effects, then the benefits of brachial plexus blockade are amplified.

During the review of the literature it was noted that there were several articles published by investigators evaluating the effects of opioids added to intermediate and

long acting local anesthetic. The investigators of this study chose to evaluate the effect of preservative free (PF) morphine added to a mepivacaine local anesthetic solution because it had the potential to provide an adequate length of surgical anesthesia without masking the analgesic effects of PF morphine during the postoperative period. Preservative-free morphine was chosen because there was a risk of an intrathecal injection with the interscalene approach to the brachial plexus. The administration of a preservative intrathecally is contraindicated due to potential neurotoxic complications.

The dose chosen for PF morphine was also based on a review of the literature. Viel, Eledjam, De La Coussaye, and D'athis (1989) studied the addition of 50 mcg/kg of morphine with 40 ml of 0.5% bupivacaine injected into the brachial plexus sheath using the supraclavicular approach. The investigators noted that the duration of postoperative analgesia was 18.25 +/- 1.15 hours. As stated earlier in the chapter, Bourke and Furman (1993) found that the addition of 0.1 mg/kg (100 mcg/kg) of morphine to a 1.5% lidocaine solution with 1:200,000 epinephrine to the brachial plexus sheaths of subjects who underwent surgery of the upper extremity consumed fewer analgesic capsules than subjects who received the local anesthetic solution alone ($p < 0.05$). According to Bazin et al. (1997), the addition of 75 mcg/kg of morphine to a 1% lidocaine and 0.5% bupivacaine solution with 1:200,000 epinephrine provided a mean delay in the onset of postoperative pain of 21 hours, with a range of 9 - 27 hours. Based on the above research, the authors of this study chose to use 75 mcg/kg of PF morphine.

Statement of the Problem

Will the preoperative injection of 75 mcg/kg of preservative free morphine and 1.5% mepivacaine with 1:200,000 epinephrine into the brachial plexus sheath of patients

receiving surgery to the hand, forearm, proximal arm, or shoulder affect the onset of postoperative pain when compared to 1.5% mepivacaine with 1:200,000 epinephrine?

Conceptual Framework

The conceptual framework for this study was derived from the science of physiology and pharmacology. According to Berne and Levy (1996), physiology is a branch of science primarily concerned with the regulatory mechanisms of individual organ systems and cells. Pharmacology is defined by Benet (1996) as an extensive science of drugs based on physical and chemical properties, biochemical and physiologic effects, mechanisms of action, absorption, distribution, biotransformation, excretion, and therapeutic uses in a living organism. The physiologic and pharmacologic model represented a solid base for the use of opioids in brachial plexus anesthesia.

According to Polit and Hungler (1995), the conceptual framework provides direction for the analysis of interrelated concepts that comprise a research hypothesis. The principle concepts requiring analysis in this study are addressed. These concepts include surgery, brachial plexus anesthesia, postoperative pain, and demographics (see Figure 1).

Surgery

According to Thomas (1993), surgery is a branch of medicine concerning diseases and trauma requiring an operative procedure. Surgery to the hand, forearm, upper arm, and shoulder lends itself to the use of brachial plexus anesthesia to provide adequate surgical anesthesia. An axillary or interscalene anesthetic may be appropriate for hand and forearm surgery. An interscalene anesthetic is especially effective for surgery involving the shoulder and/or upper arm.

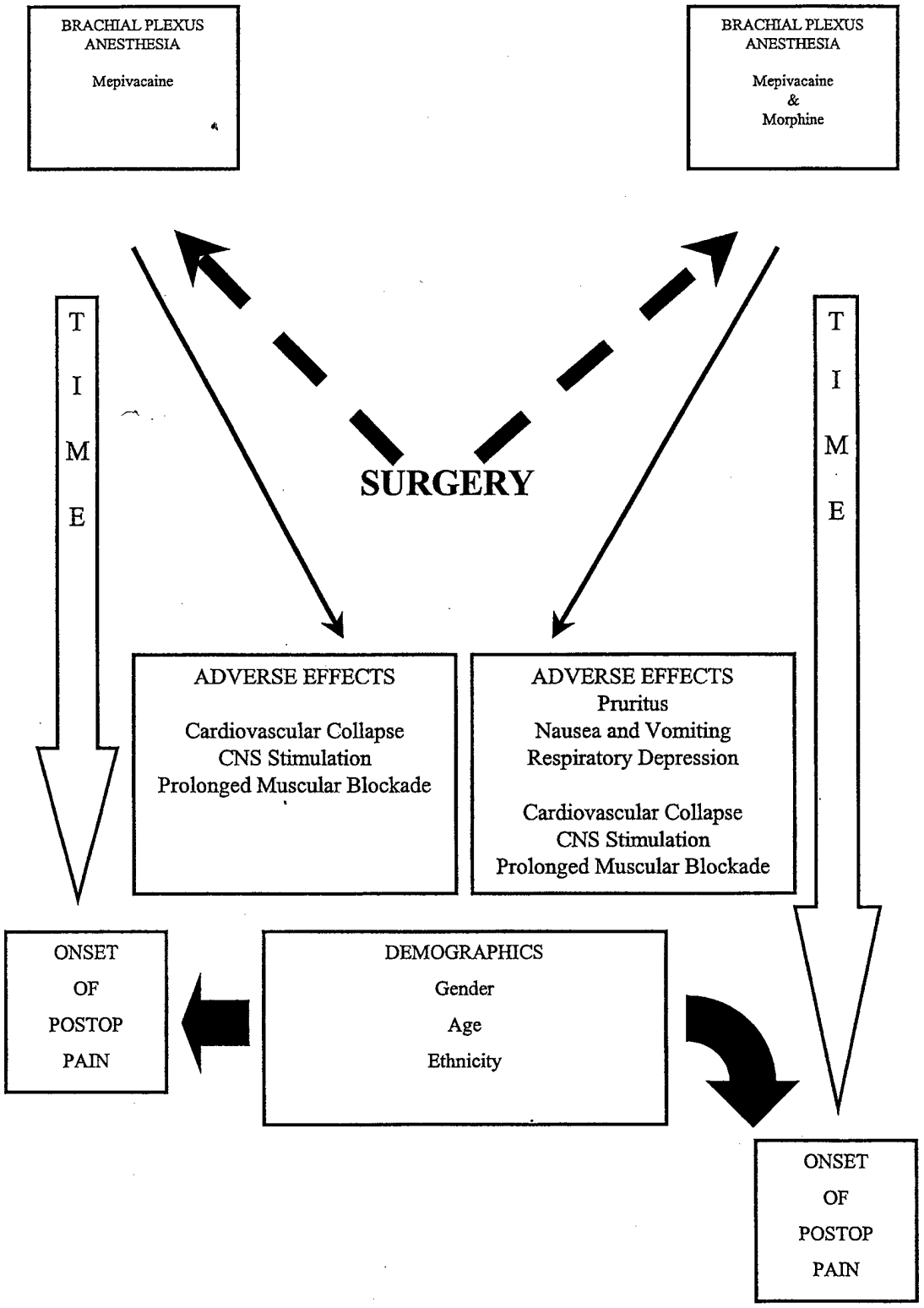

Figure 1. A physiologic and pharmacologic model with the expected effect of an opioid added to a brachial plexus anesthetic solution.

Brachial Plexus Anesthesia

The interscalene, axillary, infraclavicular, and supraclavicular approaches to the brachial plexus are commonly used for the provision of regional anesthesia (Brown, 1994). In addition, the literature supports new and less frequently used approaches to include the transcoracobrachial and orthoganol techniques (Pippa et al., 1992; Rucci, Pippa, Boccaccini, & Barbagli, 1995). When performed correctly, brachial plexus anesthesia can provide surgical anesthesia, analgesia, vasodilation, and increased warmth at any site along the length of the upper extremity (Urmey, 1996).

Anatomically, the brachial plexus is composed of nerve roots, trunks, divisions, cords, and branches. The plexus originates from the fifth cervical vertebra (C5) and extends to the first thoracic vertebra (T1). Due to variability between individuals, occasionally the fourth cervical vertebra (C4) and/or the second thoracic vertebra (T2) is included. Fascia arising from the prevertebral area, anterior scalene muscle, and middle scalene muscles surround the nerve roots. The fascia is continuous with the cervical plexus.

For surgeries involving the shoulder, the interscalene approach is preferred because it provides interruption of nerve impulses conducted through nerve roots C4 to T1. The axillary approach provides anesthesia for surgeries of the forearm and hand by blocking nerve impulse conduction through the median, ulnar, and radial nerves. The medial brachial cutaneous, intercostobrachial, and musculocutaneous nerves are not consistently blocked with the axillary approach. A ring block and an additional injection of the local anesthetic solution administered into the body of the coracobrachialis muscle is required to anesthetize these nerves (Winnie, 1990).

The injection of a local anesthetic, such as mepivacaine, into the brachial plexus provides surgical anesthesia. Local anesthetics are drugs that prevent or relieve pain by interrupting nerve conduction (Catterall & Mackie, 1996). Mepivacaine is an intermediate acting amino amide that was introduced in 1957. According to Omoigui (1995), mepivacaine is appropriate for procedures requiring a local anesthetic of intermediate duration (2 - 5 hours) and fast onset (5 - 15 minutes).

The mechanism of local anesthetic action is the direct blockade of voltage-gated sodium (Na^+) channels. When local anesthetics bind to the hydrophobic amino acid residues near the center and intracellular end of the S6 segment in domain IV, permeability to Na^+ is reversibly inhibited (Catterall & Mackie, 1996). Local anesthetics can only enter the Na^+ channels when they are in the open or active states (Catterall & Mackie, 1996).

Voltage-gated Na^+ channels are ubiquitous throughout the body. Therefore, local anesthetics can elicit adverse effects in the central nervous system (CNS), cardiovascular system, neuromuscular junction, ganglionic synapse, and smooth muscle (Catterall & Mackie, 1996). These adverse effects may include CNS stimulation, cardiac toxicity, prolonged skeletal muscle blockade, sympathetic nervous system paralysis, and hypersensitivity reactions.

Local anesthetics are divided into three groups based on potency and duration of action. Group I includes agents with low potency and a short duration of action, such as chloroprocaine and procaine. Group II agents, such as lidocaine and mepivacaine, are characterized by intermediate potency and duration. Group III agents, which have the highest potency and longest duration of action, include bupivacaine and tetracaine

(Veering, 1996). When choosing a specific local anesthetic, the anesthesia care provider must consider speed of onset, potency, duration of action, differential blockade of sensory and motor fibers, and the potential for adverse effects (Veering, 1996).

Following the effective duration of the local anesthetic (mepivacaine) in the postoperative period, the patient will experience pain. The intensity and characteristic of this pain will vary between subjects. The addition of preservative free morphine to the local anesthetic solution before surgery will delay the onset of postoperative surgical pain.

The term opioid is used to designate a group of drugs that are opium or morphine like. Opium was extracted in an impure form from the juice of the poppy seed. Originally, opioids only included the different extracts from opium such as morphine and codeine. As technology advanced, the opioid drug classification broadened to include synthetic derivatives that have agonist or antagonist morphine-like actions. Opioids share some of the properties of three neuropeptides families: the enkephalins, endorphins, and dynorphins. The neuropeptides are known as endogenous opioids (Reisine & Pasternak, 1996). According to Pasternak (1993), morphine is considered the prototype opioid or "gold standard" to which exogenous opioid analgesics are compared. The primary mechanism of morphine-induced analgesia is mediated in the central nervous system at spinal and supraspinal sites (Reisine & Pasternak, 1996). Morphine binds to mu, kappa, and delta receptors located on the terminals of primary afferent nerves, postganglionic neurons, postsynaptic interneurons, and output neurons of the spinothalamic tract (Reisine & Pasternak, 1996).

The coupling of morphine with mu, kappa, and delta receptors triggers the

activation of inhibitory guanosine 5- triphosphate (GTP) binding proteins, inhibition of adenylyl cyclase activity, activation of potassium (K^+) currents, and suppression of voltage-gated calcium (Ca^{2+}) currents (Reisine & Pasternak, 1996). This cascade of events hyperpolarizes the cell membrane and inhibits the release of presynaptic neurotransmitters, such as substance P, which are responsible for transmission of postsynaptic pain. Consequently, the frequency of action potential transmission through small diameter myelinated fibers and unmyelinated C fibers is reduced (Reisine & Pasternak, 1996).

In addition to opioid activity in the CNS, researchers have demonstrated its activity in the periphery. In the peripheral nervous system, there is strong evidence to support the existence of three heterogeneous opioid receptor populations: mu, kappa, and delta (Stein et al., 1988). Several mechanisms may be responsible for analgesia following peripheral administration of morphine. In a study conducted by Young, Wamsley, Zarbin, and Kuhar, (1980), it was demonstrated that axonal and dendritic flow of opioid receptors might be responsible for peripherally obtained opioid analgesia. Peripherally administered opioids may also exert their actions via proximal diffusion or active transport to the substantia gelatinosa (Bourke & Furman, 1993). Furthermore, the authors also cited transportation within or diffusion along sympathetic nerves to the stellate and thoracic sympathetic ganglia and systemic uptake as possible mechanisms of action (Bourke & Furman, 1993).

Although the use of opioids is supported in the literature, the anesthesia care provider must be aware of the adverse effects associated with their administration. The adverse effects range in severity from respiratory depression to nausea, vomiting, and

pruritus. Although these effects are possible with brachial plexus anesthesia, their severity and frequency will be less severe than those seen with systemic or central administration because significantly smaller doses of opioids are deposited into the brachial plexus sheath (Joris, Dubner, & Hargreaves, 1987).

Postoperative Pain

During the postoperative period, after the effective duration of the local anesthetic, the patient will experience pain related to surgical trauma. Pain results from activation of nociceptors (afferent nerve fibers designed to carry pressure, temperature, and chemical stimulus to the central nervous system) in the vicinity of injured tissues, such as that which occurs with surgery. Normal pain perception is dependent on specialized neurons that function as receptors detecting the stimulus and then conducting it into the central nervous system (Davis, 1993). Pain may result in adverse physiologic effects on the organ systems of the body. These effects can give rise to significant clinical outcomes (see Table 1). The administration of an analgesic before a painful stimulus (preemptive analgesia) may potentate the effect of subsequent analgesia (Kehlet & Dahl, 1993).

Demographics

Demographics provide information about the statistical characteristics of the human population studied (Polit & Hungler, 1995). These categories include: gender, age, marital status, religion, ethnicity, level of education, health status, and diagnosis. Any one of these factors may have an influence on the outcome of a medical study. Based on the review of literature for this study, gender, age, and ethnicity were considered due to their respective effects on pain.

Table 1

Adverse physiologic sequelae of pain

Organ System	Clinical Effect
RESPIRATORY	
Increased skeletal muscle tension	Hypoxemia
Decreased total lung compliance	Hypercapnia, V/Q abnormality,
Atelectasis, Pneumonitis	
ENDOCRINE	
Increased adrenocorticotropic hormone	Protein catabolism
Increased cortisol	Lipolysis, CHF
Increased glucagon	Hyperglycemia
Increased epinephrine	
Decreased insulin	
Decreased testosterone	Decreased protein anabolism
Increased aldosterone	Salt and water retention
Increased antidiuretic hormone	
Increased catecholamines	Vasoconstriction
Increased angiotensin II	Increased myocardial contractility, Increased HR
CARDIOVASCULAR	
Increased myocardial work	Dysrhythmias, Angina, Myocardial Infarction, Congestive Heart Failure
IMMUNOLOGIC	
Lymphopenia	Decreased immune function
Depression of reticuloendothelial system	
Leukocytosis	
Reduced T-cell cytotoxicity	
COAGULATION EFFECTS	
Increased platelet adhesiveness	
Diminished fibrinolysis	
Increased incidence of thromboembolic phenomena	
Activation of coagulation cascade	
GASTROINTESTINAL	
Increased sphincter tone	Ileus
Decreased smooth muscle tone	

GENITOURINARY	
Increased sphincter tone	Urinary retention
Decreased smooth muscle tone	

Note. From Clinical Anesthesia (p. 1310), by P. F. Cullen, and R. K. Stoelting (Eds.), 1997, Philadelphia: Lippincott-Raven. Copyright 1997 by Lippincott-Williams & Wilkins. Reprinted with permission.

Purpose

The purpose of this study was to compare the onset of postoperative surgical pain following surgery to the hand, forearm, arm, and/or shoulder in patients who received 75 mcg/kg of preservative free morphine combined with a 1.5% mepivacaine and 1:200,000 epinephrine solution to the brachial plexus sheath prior to surgery with patients who received a 1.5% mepivacaine and 1:200,000 epinephrine solution to the brachial plexus sheath prior to surgery.

Definition of Terms

Analgesia

Conceptual Definition. Analgesia is an alteration in the perception of nociceptive stimuli without accompanying anesthesia or loss of consciousness (Hensyl, 1990).

Operational Definition. Analgesia is a perceived decrease in the level of pain as assessed by the subject's verbal description and numeric rating of pain.

Brachial Plexus Anesthesia

Conceptual Definition. Brachial plexus anesthesia is the application of a local anesthetic solution into the brachial plexus nerve sheath to provide surgical anesthesia, analgesia, and increased warmth and vasodilation within the length of the shoulder and upper extremity (Urmey, 1996).

Operational Definition. Brachial plexus anesthesia, using the axillary and/or interscalene/general endotracheal anesthesia (GETA) approaches, is the provision of surgical anesthesia as verified by the anesthesia care provider and surgeon through the application of noxious tactile stimulation to the intended area of surgery.

Failed Block

Conceptual Definition. A failed block is the absence of brachial plexus anesthesia in the intended surgical region of the hand, forearm, proximal arm, and/or shoulder.

Operational Definition. A failed block is brachial plexus anesthesia in which there is maintenance of motor and sensory function in the intended surgical region of the upper extremity as determined by the anesthesia care provider's perioperative assessment.

Onset of Postoperative Pain

Conceptual Definition. The onset of postoperative pain is the manifestation of an unpleasant sensory and emotional experience associated with tissue damage related to the surgical procedure.

Operational Definition. The onset of postoperative pain is the appearance of an unpleasant sensation related to the surgical procedure as evidenced by the subject's report.

Partial Block

Conceptual Definition. A partial block is incomplete brachial plexus anesthesia with lack of analgesia and motor blockade in one or several regions of the hand, forearm, proximal arm, and/or shoulder.

Operational Definition. A partial block is incomplete brachial plexus anesthesia with randomized areas of motor and sensory dysfunction as evidenced by the patient's incomplete ability to extend and flex the elbow, adduct all fingers, and oppose middle, forefinger, and thumb.

Postoperative Period

Conceptual Definition. The postoperative period is the 72 hour period of time immediately following surgery.

Operational Definition. The postoperative period is the period extending from wound closure to the time that the investigators contact the patient (up to 72 hours following surgery) to collect information concerning the onset of postoperative pain and sensory and motor function.

Successful Block

Conceptual Definition. A successful block is brachial plexus anesthesia in which all nerves of the intended surgical region in the hand, forearm, proximal arm, and/or shoulder are anesthetized, resulting in no motor or sensory function in that area.

Operational Definition. A successful block is brachial plexus anesthesia with the absence of motor and sensory function in the intended surgical region as evidenced by the ability to continue surgery without the need for supplemental analgesics or local anesthetics in response to surgical stimulation.

Primary Hypothesis

The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, arm, and/or shoulder will delay the onset of postoperative surgical pain longer than a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

Secondary Hypotheses

1. The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine

with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, and/or shoulder will alter the return of sensory function when compared to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

2. The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, and/or shoulder will alter the return of motor function when compared to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

Additional Analysis

In addition to the primary and secondary hypotheses the investigators analyzed additional data. The investigators evaluated the differences in the character and intensity of postoperative pain between the treatment and control groups. The investigators evaluated the difference in the amount of supplemental analgesics consumed postoperatively by the treatment and control groups.

Significance of the Problem

Successful brachial plexus anesthesia provides reliable surgical anesthesia to patients undergoing surgery of the upper extremity and shoulder. This is demonstrated by the fact that various surgical procedures can be performed on the upper extremity and shoulder without requiring the administration of additional analgesics. Standard local anesthetics applied to the brachial plexus provide anesthesia during the surgical period, but these anesthetics may not provide reliable extended postoperative analgesia. Reliable postoperative analgesia is not consistently obtained with certain local anesthetics when

the duration of action of the local anesthetics does not extend beyond the duration of the surgical procedure. Postoperative analgesia can be provided by parenterally administered opioids. However, the incidence of side effects, such as nausea and vomiting, associated with central administration of opioids are common. Because the application of opioids to the brachial plexus may extend postoperative analgesia while minimizing systemic side effects, it is a promising approach to managing postoperative surgical pain.

Assumptions

Assumptions in this study were as follows:

1. A delay in the onset of postoperative pain was associated with improved patient satisfaction.

2. Surgery of the hand, forearm, arm, and/or shoulder was associated with postoperative pain.

3. The subjects were able to differentiate between pressure and pain and report postoperative pain accurately.

4. If a subject did not complain of postoperative pain, the subject did not experience pain.

5. Once the subject complained of pain and received medication, this medication did not interfere with assessment of sensory and motor function.

6. Brachial plexus anesthesia resulted in the loss of sensory function (pain fibers) followed by the loss of motor function. The return of function occurred in the opposite order.

7. The assessment of motor, sensory, and pain sensations experienced by the subject accurately reflected the actions of medications used in the study.

8. The duration of action of mepivacaine in the brachial plexus was 3 to 5 hours.

9. The return of sensory and motor function in the absence of pain, beyond the duration of action of mepivacaine, reflected the action of morphine.

10. Stable vital signs and a decrease in the quantity of anesthetic agents required reflected a successful interscalene brachial plexus block.

11. All staff involved in the study complied with the set guidelines and document data accurately.

Limitations

Limitations in this study were as follows:

1. The use of convenience sampling limited generalizability. Demographic data were gathered and the sample was described.

2. The method of administering brachial plexus anesthesia was not randomized. The approach was determined by the anesthesia care provider and depended which approach was most appropriate for the subject. It was unethical to randomize the approach; therefore any differences between the groups are described in the discussion section.

3. Only the brachial plexus block solution administered was standardized. The effects of other medications administered perioperatively was not controlled. The anesthesia care provider was asked to list all intraoperative agents used, and all postoperative pain medications given to the subject were documented.

4. Only one concentration of mepivacaine, epinephrine and morphine was used. Therefore, conclusions can be generalized only to these concentrations.

5. Differences between subjects could not be controlled, such as type and length of surgery, coexisting disease processes, and response to anesthesia. These differences

varied with the length of time spent in the operating room, post anesthesia care unit (PACU), and ambulatory surgery center (ASC). Therefore, exact times could not be set for data collection points. To control data collection, assessments were standardized to the subject's flow through the health care facility and discharge to home. In addition, an assessment was performed upon the subject's first report of pain.

6. Data was collected by more than one researcher. To increase interrater reliability, all data were collected on the tools developed for the study, and scripts were used for all teaching and telephone communications. In addition, interrater reliability testing was performed.

7. The inability to contact study subjects via telephone led to attrition. A follow up phone call occurred at a set time, and the subject was aware of this time prior to leaving the hospital. If the subject could not be reached at this time, guidelines were followed for further attempts to contact the subject.

Summary

The use of brachial plexus anesthesia is a reliable alternative to general anesthesia for surgical procedures performed on the upper extremity and/or shoulder. The potential to extend postoperative pain relief to patients receiving a brachial plexus anesthetic offers many benefits to the patient and the health care system. Currently, studies support and negate the ability of an opioid to delay the onset of postoperative pain when administered in the brachial plexus.

This study was conducted to compare the onset of postoperative surgical pain following surgery to the hand, forearm, arm and/or shoulder in patients who received either a 75 mcg/kg preservative free morphine with 1.5% mepivacaine and 1:200,000

epinephrine solution or a 1.5% mepivacaine with 1:200,000 epinephrine solution into the brachial plexus sheath prior to surgery. The investigators used a pharmacological and physiological model as the conceptual framework for this study. Further data on the addition of opioids to a brachial plexus anesthetic to delay the onset of postoperative pain is needed to assist anesthesia care providers in making informed decisions related to postoperative pain management.

CHAPTER II

Review of Related Literature

The concept of augmenting regional anesthesia with opioids is not new. The use of opioids in the subarachnoid space has gained widespread acceptance, but the central side effects, such as respiratory depression and pruritis, remain (Cousins, Cherry, & Gourlay, 1988). The discovery of opioid receptors in the peripheral nerve tissue, as well as in the sympathetic ganglia, has prompted exploration of new sites for opioid injection (Kardash, Schools, & Concepcion, 1995). Reports of successful use of perineural opioid injection in the treatment of chronic pain patients (Mays, Lipman, & Schnap, 1987; Sanchez, Nielsen, Heslet, & Iversen, 1984) has led to the investigation of their use for postoperative pain relief.

The purpose of this chapter is to explore the question: Does the addition of 75 mcg/kg of PF morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, and/or shoulder delay the onset of postoperative surgical pain longer than a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath. This chapter includes a discussion of pain, the brachial plexus, anesthetic approaches used to block the brachial plexus, evaluation of motor and sensory block, local anesthetics, and opioids. Conflicting research involving the use of opioids with local anesthetics at peripheral sites is reviewed.

Pain

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or

awareness and cognizance that provides the anesthesia provider an estimation of the experienced discomfort. Ultimately, a patient's pain is what the patient says it is.

Pain results from activation of nociceptors in the vicinity of injured tissues such as that which occurs with surgical trauma. Like other conscious sensations, normal pain perception is dependent on specialized neurons that function as receptors, detecting the stimulus and then conducting it into the central nervous system (Davis, 1993). Anesthesia care providers must be aware that the pain response can be highly variable between individuals as well as in the same individual on different occasions.

Cultural or ethnic background has been associated with variations in pain intensity reports (Bates, Edwards, & Anderson, 1993; Lipton & Marbach, 1984). Bates et al. (1993) studied the role of ethnocultural experiences in 372 chronic pain patients from six different ethnic groups. These researchers looked at physical, cultural, and psychosocial factors that influence pain. From their findings, they concluded that attitudes and emotions influence pain. Furthermore, these parameters varied among different ethnic groups. Hispanics were more expressive about their pain. Polish and Old World Americans (described as the culture that dominates the U.S. medical system) were least expressive about their pain ($p < 0.05$).

Gender is another factor that has been associated with pain perception. Raftery, Smith-Coggins and Chen (1995) found that female patients seen in the Emergency Department described more pain than male patients ($p < .01$, $n = 190$). These investigators also suggested that female patients were perceived by the providers as having more pain ($p = .03$). DePalma and Weisse (1997) prepared an overview of how psychological variables impact the pain experience. They pointed out that in most studies there was a tendency for females to report higher levels of pain than their male

counterparts when all subjects were administered the same painful stimuli in a laboratory setting.

Age is a third factor that has been associated with pain perception. As children develop, they go through stages in which they understand more about the process of pain. Younger children tend to report more pain than older children (DePalma & Weisse, 1997). Harkins, Kwentus, and Price (1990) stated that the central nervous system undergoes progressive and global decreases in the transmission of afferent impulses in the geriatric patient. However, it is unlikely that this diminishes pain perception. It is more likely that because of a nearly linear decline in visual and auditory acuity, the elderly report pain differently. Because of this, the elderly tend to be under-medicated for pain (Bonica, 1990).

Pain also differs between chronic and acute pain. Chronic pain is caused by long standing pathologies to somatic or visceral structures. It can also have components of peripheral and/or central nervous system dysfunction. It is different from acute pain in that chronic pain can also be caused by psychological mechanisms and/or environmental factors (Bonica, 1990). It is more difficult to treat chronic pain than acute pain because the mechanisms for chronic pain are less understood.

At least three factors contribute to the difficulty of measuring clinical chronic or acute pain. First, the pain experience is subjective. Only the person experiencing the pain can accurately define that pain. Many practitioners are unsatisfied because those subjective reports cannot be verified (McGuire, 1983). Another factor is difficulty in quantifying the pain. Likert scales quantify data, but they do not measure the entire pain experience (McGuire, 1983). A third factor is the reliability and validity of the instrument used to measure pain.

Pain measurement instruments vary from unidimensional to multidimensional tools. Three unidimensional tools are the Numerical Rating Scale (NRS), the Verbal Descriptor Scale (VDS), and the Visual Analogue Scale (VAS). These unidimensional instruments are used to measure intensity and unpleasantness of pain (Duncan, Bushnell, & Lavigne, 1989). The McGill Pain Questionnaire is a multidimensional instrument that measures location, sensation, evaluation, intensity, and pattern of pain.

The NRS, described by Downie in 1978, allows the subject to rate his or her pain intensity on a scale from 0 to 10 (Flaherty, 1996). Zero indicates no pain, while 10 indicates the worst pain ever experienced by the subject. Currently, there are multiple versions of this scale ranging from a verbal explanation to a line that is oriented either horizontally or vertically and is labeled at each end with the numbers zero and ten. None of these versions have proven to be superior to the others (Flaherty, 1996).

The NRS is simple to administer, easy to score, and readily available (Flaherty, 1996). The nurses in the Post Anesthesia Care Unit at the medical center in which this study was conducted used the NRS to evaluate the intensity of patient reported pain. Limitations of this scale include the use with extremes of ages, impaired cognition, and the inability to differentiate between numbers (Flaherty, 1996). For example, a heavily sedated elderly patient or young child may not be able to express his or her pain using a numerical value. The investigators did not find the current validity and reliability of the NRS.

Brachial Plexus

The brachial plexus is composed of nerve roots, trunks, divisions, cords, and branches. The plexus originates from the fifth cervical vertebra and extends to the first thoracic vertebra (Urmey, 1996). The fourth cervical vertebra or the second thoracic

vertebra may be included. Fascia arising from the prevertebral area, anterior scalene muscle, and middle scalene muscle surrounds the nerve roots. The fascia is continuous with the cervical plexus (Urmey, 1996).

Fusion of the nerve roots forms the upper, middle, and lower nerve trunks. As the neural bundle passes between the clavicle and first rib, it joins the subclavian artery and becomes the neurovascular bundle. The anesthesia care provider uses the subclavian and axillary arteries as valuable landmarks when administering brachial plexus anesthesia (Urmey, 1996).

The trunks further divide into anterior and posterior divisions that form cords named according to their anatomical relationship to the axillary artery. The lateral, medial, and posterior cords form the terminal branches at the level of the axilla. The musculocutaneous nerve arises from the lateral cord. The median nerve originates from the lateral and medial cords. The ulnar, medial antebrachial cutaneous, and medial brachial cutaneous nerves are formed from the medial cord. The axillary and radial nerves originate from the posterior cord. The intercostobrachial nerve is formed from the second thoracic nerve root. Although not included in the brachial plexus, blockade of this nerve is critical when performing shoulder surgeries (Urmey, 1996). The nerves of the brachial plexus provide sensory innervation to the upper extremity (see Figure 2).

The median, musculocutaneous, radial, ulnar, and axillary nerves supply motor innervation to the upper extremity and shoulder. Stimulation of the median nerve produces pronation of arm, flexion of the wrist, opposition of the middle forefinger and thumb, and flexion of the lateral three fingers. Flexion of the elbow results from extension of the elbow, supination of the arm, and extension of the wrist and fingers. Flexion of the wrist, adduction of all fingers, and flexion and opposition of the lateral

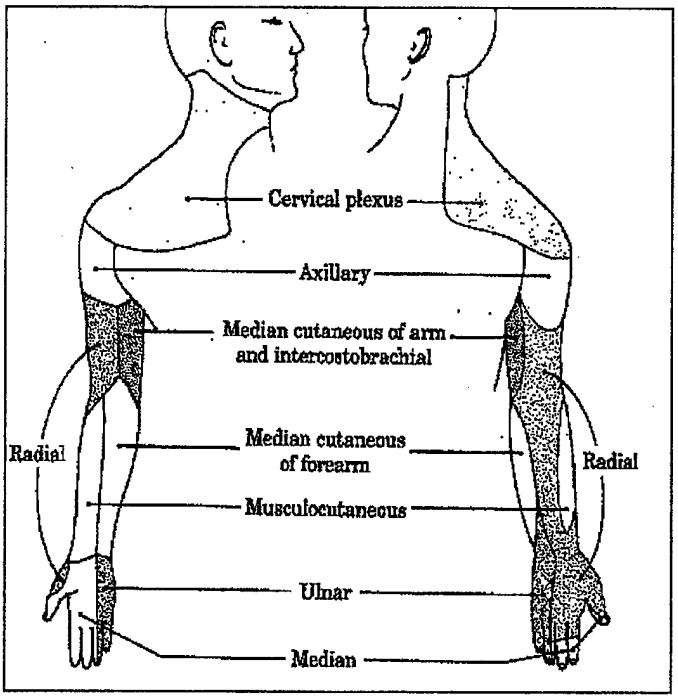

Figure 2. Sensory innervation of the upper extremity

Note. From Clinical Anesthesia Procedures of the Massachusetts General Hospital (p. 270), by W. E. Hurford, M. T. Bailin, J. K. Davison, and C. Rosow, 1998, Philadelphia: Lippincott-Raven.

two fingers toward the thumb results from stimulation of the ulnar nerve. Adduction of the shoulder results from stimulation of the axillary nerve (Bridenbaugh, 1988).

Anesthetic Approaches

According to Brown (1994), there are many approaches to the brachial plexus for the provision of regional anesthesia. The approaches commonly used are axillary, interscalene, infraclavicular, and supraclavicular (Brown, 1994). The axillary and interscalene approaches will be the focus of this study.

Axillary Approach

According to Urmey (1996), the most popular approach used to block the brachial plexus is the axillary approach. Hirschel first described the axillary block in 1911 (Winnie, 1990). Since then, the approach has been modified extensively. For an axillary block, the anesthesia care provider uses the axillary artery as a landmark for injection of the block solution. The injection site is not near the lung, subarachnoid space, phrenic nerve, or stellate ganglion; therefore, there is less risk of major complications (Brown, 1994; Urmey, 1996). Schroeder, Horlocker, and Schroeder (1996) retrospectively reviewed 330 surgical procedures in 260 patients to evaluate the success rates of interscalene, supraclavicular, and axillary blocks for procedures below the elbow. Of the 330 surgical procedures, 156 involved a bony prominence. Success was defined as the ability of the surgery to continue without supplemental nerve block or general anesthesia. The axillary approach was used in 247 of the cases with an overall success rate of 89% compared to a 78% and 75% success rate with the supraclavicular and interscalene approaches, respectively ($p < 0.025$). The axillary approach is safer than other approaches. However, an awareness of its potential limitations and complications is important. According to an editorial by Winnie (1995), a primary disadvantage in using

the axillary block is failure to provide adequate anesthesia to the surgical field. This is because the musculocutaneous nerve may leave the sheath proximal to the site of injection. The musculocutaneous nerve is important because it provides motor innervation to the coracobrachialis and biceps muscles and sensory innervation to the lateral aspect of the forearm (Urmey, 1996).

Thompson and Rorie (1983) studied the brachial plexus in three adult cadavers using anatomic dissection, histology, and radiographic imaging. Fascial compartments surrounding individual nerves in the brachial plexus were identified. Through radiographic dye studies, the authors concluded that these compartments define the boundaries of the nerve and limit the circumferential spread of local anesthetics injected into the axillary sheath. These anatomical features may be responsible for an unknown percentage of failed axillary blocks using the single injection approach (Thompson & Rorie, 1983).

Partridge, Katz, and Benirschke (1987) confirmed the existence of these fascial compartments. In contrast to Thompson and Rorie (1983), they distinguished connections between the compartments that allowed longitudinal spread of an injected local anesthetic. This evidence supports the single injection technique of a local anesthetics. (Partridge et al., 1987).

Techniques of Axillary Anesthesia

Axillary brachial plexus anesthesia can be achieved with the commonly used paresthesia, nerve stimulator, and transarterial techniques. Each technique has advantages and disadvantages. Yamamoto, Tsubokawa, Shibata, and Kobayashi (1995) conducted a prospective study of 222 consecutive adult patients scheduled to receive an axillary anesthetic via the paresthesia technique. The investigators demonstrated that

conduction in each nerve was blocked with the highest reliability after paresthesia occurred in the region supplied by that nerve. The authors speculated that the single paresthesia technique may be more efficient than transarterial injections or multiple paresthesias. Eliciting of paresthesias is a sign of correct needle position, but this technique theoretically poses the risk of an increased incidence of post anesthetic neuropathy (Urmey, 1996).

A peripheral nerve stimulator can be used to establish that the needle is close enough to the nerve for reliable anesthesia (Greenblatt & Denson, 1962). Using a double-blind randomized design, Koscielniak-Nielsen, Stens-Pedersen, and Lippert (1997) studied 80 patients scheduled for an axillary anesthetic using the peripheral nerve stimulator technique. The mean time to perform the single injection technique was 5.5 minutes, which was 4 minutes faster than multiple injections ($p < 0.0001$). The onset of its effect was reported to be 33 minutes for the single injection group, which was 17.5 minutes longer than the multiple injection group ($p < 0.0001$). The single injection group required supplemental nerve block for 57% of the cases compared to only 7% in the multiple injection group ($p < 0.0001$). The multiple injection group was prepared for surgery in 25 minutes; this was 13.5 minutes faster than the single injection group ($p < 0.0001$). Despite the relative speed and simplicity offered by the single injection technique, success rate of this technique was between 59% and 83%. The presence of fascial compartments may be responsible for this low success rate (Thompson & Rorie, 1983). Failed anesthesia with this technique may also be due to stimulation outside of the fascia or direct muscle stimulation (Urmey, 1996).

The transarterial technique involves needle insertion through the axillary artery until no further blood is aspirated. At this point, the local anesthetic is injected (Aanta,

Kirvela, Lahdenpera, & Nieminen, 1994). Stan, Krantz, Solomon, Poulos, and Chaouki (1993) conducted a prospective study of 1,000 consecutive patients receiving axillary anesthesia using the transarterial technique. Stan et al. studied the frequency of neurologic and vascular complications to assess safety and success rate. Neurologic complications included sensory paresthesia of the ulnar and musculocutaneous nerve (0.2%), upper-arm myalgias (0.3%), and reflex sympathetic dystrophy (0.2%). Vascular complications included transient arterial spasm (1%), intravascular injection (0.2%), and hematoma formation (0.2%). Successful anesthesia occurred in 88.8% of the cases, incomplete anesthetic in 10%, and complete failure in 1.2%. Stan et al. concluded that the transarterial technique is a safe and effective approach to the brachial plexus.

Jones (1997) compared success rate in locating the brachial plexus using the peripheral nerve stimulator and transarterial techniques. Success was defined as anesthesia to the nerves supplying the surgical field. A sample of 57 patients scheduled for upper extremity surgery was randomized to receive axillary anesthesia. Sensory and motor blockade on the musculocutaneous, radial, and ulnar nerves was similar. A difference between techniques in blocking the axillary nerve existed. The transarterial technique provided effective anesthesia in the area of the axillary nerve 66% of the time compared to 47% with the peripheral nerve stimulator ($p < 0.05$). Jones concluded that both techniques are equally effective. The use of fentanyl and midazolam as operative premedications may have influenced the perceived effectiveness of sensory and motor blockade.

Disadvantages of the transarterial approach include potential for hematoma formation with accompanying nerve compression. Another complication is inadvertent intravascular injection. This can be avoided by frequent aspiration to check for blood

prior to injection (Urmey, 1996).

Interscalene Approach

The interscalene approach to the brachial plexus is effective for surgical procedures involving the shoulder and/or upper extremity because the anesthetic solution is deposited at the level of the brachial plexus roots. This technique was first described by Winnie in 1970, and only minor modifications have been made in the technique since that time (Urmey, 1996). The technique can be performed using paresthesias or a nerve stimulator to determine the needle position near the plexus. The patient's arm can be in almost any position. An advantage is that almost all patients have easily identifiable scalene muscles and vertebral body anatomy (Brown, 1994). Potential problems from an interscalene anesthetic include subarachnoid injection resulting in a total spinal anesthetic, epidural blockade, intravascular injection resulting in seizures, pneumothorax, phrenic nerve block causing hemidiaphragmatic paresis, recurrent laryngeal nerve block causing hoarseness, and cervical sympathetic block presenting as Horner's Syndrome (Brown, 1994; Sukhani, Barclay, & Aasen, 1994).

In a case reported by Passannante (1996), a patient sustained permanent neurologic damage of the medial cord with minimal damage to the posterior cord following a nerve stimulator-guided interscalene anesthetic. Although the exact mechanism of injury could not be determined retrospectively, a subarachnoid injection was presumed. Additionally, the author suggested injecting the anesthetic in an awake patient who could react if an injection was administered intraneurally. Authors of another case report described prolonged Horner's Syndrome following an interscalene anesthetic (Sukhani et al., 1994). The proposed topical application of direct acting sympathomimetics, such as phenylephrine, failed to correct the ocular manifestations.

An interscalene brachial plexus anesthesia causes a high incidence of hemidiaphragmatic paresis. Fujimura et al. (1995) investigated the effects of hemidiaphragmatic paresis and found that tidal volume, minute volume, and the partial pressure of arterial carbon dioxide were maintained. This was secondary to a compensatory increase in frequency of breathing. Urmey and McDonald (1992) concluded that interscalene anesthetics should not be performed on patients who are dependent on intact diaphragmatic function. Additionally, these authors suggested that interscalene anesthetics should be avoided in patients who are unable to tolerate a 25% reduction in pulmonary function.

Researchers have suggested that interscalene anesthetics are safe and well accepted by patients (Dorman, Conroy, Duc, Haynes, & Friedman, 1994; Tetzlaff, Yoon, & Brems, 1993). Dorman et al. (1994) demonstrated that interscalene anesthetics provided safe and effective anesthesia for shoulder surgery ($n = 20$). No local anesthetic toxicity was observed. In a study by Tetzlaff, Yoon, and Brems (1993), 24 out of 25 patients said they would prefer interscalene anesthesia to other types of anesthesia if they needed subsequent procedures.

Careful planning and thorough knowledge of the anatomy of the brachial plexus is essential for a successful brachial plexus anesthetic. Experience also contributes to the success rate of the anesthetic. Tulchinsky, Weller, Rosenblum, and Gross (1993) conducted a retrospective analysis of 367 anesthesia records. Either experienced anesthesiologists or a resident in training anesthetized the patients. Experience in performing the anesthetic increased the success rate from 90% to 98%. In addition to experience and selecting the best approach to the brachial plexus, choosing an appropriate local anesthetic is important to brachial plexus anesthesia.

Although brachial plexus anesthesia may provide adequate analgesia and anesthesia for the surgical procedure, some patients complain of pain when a pneumatic tourniquet is used for the surgery. Patients may complain of a dull ache and become restless, even under apparent adequate anesthesia. This pain is usually experienced 45-60 minutes after inflation of the tourniquet and becomes more intense with time. One explanation for this pain involves the transmission through A delta and C fibers (Wedel & Horlocker, 1997).

Evaluation of Motor and Sensory Block

According to Urmey (1996), the art of regional anesthesia entails the ability to judge the quality of anesthesia after a regional technique. There are many methods used to evaluate the adequacy of sensory and motor blockade achieved with interscalene and axillary brachial plexus anesthesia. The method used to assess sensory and motor function following the administration of a brachial plexus anesthetic should be simple to execute, expedient, and accurate.

Most investigators have used either pinprick or temperature discrimination to evaluate sensory function. Sensory innervation to the upper extremity and shoulder is supplied by branches of the axillary, musculocutaneous, radial, ulnar, median, medial brachial cutaneous, and medial antebrachial cutaneous nerves. The peripheral fields of sensory distribution for these nerves are anatomically and clinically well documented.

A numeric rating scale developed by Bromage (1976) has been used in several studies to evaluate the sensory blockade provided by brachial plexus anesthesia (Gormley, Hill, Murray, & Fee, 1996; Hickey, R., Rowley, C. L., Candido, K. D., Hoffman, J., Ramamurthy, S., & Winnie, A. P., 1991; Hickey, Rogers, Hoffman, Ramamurthy, & Tingle, 1993; Hickey et al., 1992; & Mackay & Bowden, 1997).

Investigators in these studies assessed sensory loss with a sharp object (i.e., an 18-guage needle) using a graded scale from 0 to 2 (0 = no loss of sensation to pinprick, 1 = analgesia - patient feels touch but not pinprick, 2 = no sensation of touch).

Furthermore, most investigators have used gross motor movement to evaluate motor function in the anesthetized extremity. Branches of the median, radial, ulnar, musculocutaneous, and axillary nerves supply motor innervation to the upper extremity and shoulder. Using a simple numeric rating scale developed by Bromage (1976), a rapid assessment of motor function in the upper extremity and shoulder can be performed at predetermined intervals (0 = no weakness, 1 = paresis, and 2 = paralysis) (Gormley et al., 1996; Hickey et al., 1991; Hickey et al., 1993; & Hickey et al., 1992).

Local Anesthetics

Mechanism of Action of Local Anesthetics

Local anesthetics are reversible nondepolarizing sodium channel blockers. These drugs exert their effect by preventing rapid depolarization of the cell membrane. This in turn stops nerve impulses by preventing the propagation of an action potential. Preferential block occurs when the sodium channel is open; therefore increases in nerve impulses potentiates the block. Each nerve fiber has a critical block length in which three nodes of Ranvier must be bathed in local anesthetic to ensure a complete block. Because A delta and C sensory fibers are smaller, they are blocked faster than the larger A alpha motor fibers (de Jong, 1996).

Local anesthetics are classified as either amides or esters. Amides include lidocaine, mepivacaine, bupivacaine, etidocaine, prilocaine, and ropivacaine. Esters include procaine, chloroprocaine, and tetracaine. Lidocaine and mepivacaine are used to provide anesthesia lasting 2 to 5 hours. Bupivacaine and ropivacaine are used to provide

anesthesia lasting 9 to 11 hours and analgesia up to 24 hours. Lidocaine 1.5% and mepivacaine 2% solution are administered in volumes ranging from 40 to 55 ml up to a maximal safe dose of 500 mg. These intermediate acting local anesthetics are used for most routine procedures. Bupivacaine 0.5% in addition to ropivacaine 2% solution are administered in volumes up to 40 ml with a maximal safe dose of 150 mg. These long acting local anesthetics are used for extended procedures or postoperative analgesia (Veering, 1996).

Pharmacology of Local Anesthetics

The most important characteristics in choosing the appropriate local anesthetic are onset, potency, duration, and side effects associated with individual agents. Furthermore, the anesthesia care provider must consider the percentage of protein binding and lipid solubility. The pharmacokinetics and pharmacodynamic properties of the ester and amide local anesthetics are summarized in Table 2. Data related to the protein binding and lipid solubility of chloroprocaine is not available (Stoelting, 1995).

Onset.

To be effective, local anesthetics must cross the cell membrane and enter the open sodium channel from within the cell. The drug crosses the cell membrane in the non-ionized form and once across, must become ionized to bind to the sodium channel. The amount of drug in the non-ionized form is dependent upon the disassociation constant (pKa) of the drug and the hydrogen ion concentration (pH) of the environment. Whereas the pKa is intrinsic to the drug, the pH of the environment can be manipulated. By increasing the pH, more of the drug will cross the membrane and block sodium channels (Skidmore, Patterson, & Tomsick, 1996).

Alkalinization of local anesthetics has been studied. A pH adjustment of lidocaine

Table 2

Pharmacokinetic and pharmacodynamic properties of local anesthetics

Classification	Onset	Potency	Duration (min.)	Protein Binding (%)	Lipid Solubility
Esters:					
Procaine	Slow	1	45-60	6	0.6
Chloroprocaine	Rapid	4	30-45		
Tetracaine	Slow	16	60-180	76	80
Amides					
Lidocaine	Rapid	1	60-120	70	2.9
Mepivacaine	Slow	1	90-180	77	1.0
Bupivacaine	Slow	4	240-480	95	28
Etidocaine	Slow	4	240-480	94	141
Prilocaine	Slow	1	60-120	55	0.9

Note. The investigators constructed the above table using information from assembled from Handbook of Pharmacology & Physiology in Anesthetic Practice (p. 123-144), by Stoelting, Robert, K., 1995, Philadelphia, PA: Lipincott – Raven.

using sodium bicarbonate ($n = 42$) resulted in a faster onset of action (Gormley et al., 1996). Investigators found that alkalinization of mepivacaine also resulted in a faster onset ($p < 0.05$) (Quinlan, Oleksey, & Murphy, 1992; Tetzlaff et al., 1990). In addition, the quality of both interscalene (Tetzlaff, Yoon, Brems, & Javorsky, 1995) and axillary anesthetics (Quinlan et al., 1992) were improved by alkalinization of mepivacaine ($p < 0.05$). In another alkalinization study ($n = 60$), bupivacaine did not result in faster onset ($p > 0.05$) (Bedder, Kozody, & Craig, 1988).

A faster onset not only facilitates surgical anesthesia, but also may decrease the need for additional pain medication (Gormley et al., 1996) and reduce the pain on injection (Friedman, Jules, Springer, & Jennings, 1997). The need for additional medication with brachial plexus anesthesia dropped 30% ($p = 0.03$) when lidocaine and epinephrine were buffered with sodium bicarbonate. Gormley et al. attributed the decrease in pain medication to a faster onset of the local anesthetic.

Potency.

Potency is a measure of the amount of drug required to have a desired effect. A study was done with intrathecal administration of local anesthetics in 150 mice (Langerman, Bansinath, & Grant, 1994). The investigators demonstrated that lidocaine was 2.4 times more potent than procaine. Bupivacaine was 23 times more potent than procaine. Solubility of the drug contributes to its potency. Lipid soluble drugs cross the cell membrane easier than hydrophilic drugs, which increases the potency of the drug (Veering, 1996).

Protein binding contributes to local anesthetic potency. Local anesthetics, which are bound to serum proteins, are not pharmacologically active nor are they metabolized. Therefore, local anesthetics that are extensively bound to proteins will have a longer half-

life than those that are chiefly unbound (Carpenter & Mackey, 1997).

Duration.

The duration of action is the length of time the drug exerts its effects. The longer the drug is at the target site, the longer the duration of action should be. The liver metabolizes the majority of amide local anesthetics. Their metabolism rate is primarily determined by blood flow to the liver. Ester local anesthetics are metabolized by plasma cholinesterases. Patient production of this enzyme determines the rate of metabolism. Patients who have a deficiency of this enzyme will have a prolonged duration of action when given ester type local anesthetics (Carpenter & Mackey, 1997).

Absorption of the local anesthetic into the vasculature eliminates the drug from its site of action. Vasoconstrictors have been used to decrease the rate of drug absorption and thus lengthen the duration of drug effect (Veering, 1996). Because the blood vessel is constricted, the rate of drug onset is also slower. These effects are due to the drug's activity at alpha 2 receptors (Stoelting, 1995). Mepivacaine has been shown to provide 2 to 3 hours of surgical anesthesia without epinephrine and 3 to 5 hours of surgical anesthesia with epinephrine (Veering, 1996). Liu, Carpenter, Chiu, McGill and Mantell (1995) conducted a study using 0.2 ml of either 1.5% lidocaine or 0.25% bupivacaine ($n = 6$) with epinephrine, the duration of local anesthetic action was increased by as much as 100% to 200% ($p < 0.01$). Vasoconstriction correlated to a longer duration of analgesia even with weak doses of epinephrine. The investigators of this study recommend the routine use of 1:200,000 epinephrine routinely and 1:3,200,000 epinephrine for patients who may be sensitive to epinephrine. The benefits of epinephrine are not confined to the duration of analgesia. This drug can also decrease surgical blood loss (via production of local vasoconstriction) and be an early warning of inadvertent intravenous injection of

local anesthetic (by causing a rapid increase in the patient's heart rate), which can be lethal (Veering, 1996).

Clonidine has been used experimentally to improve the duration of action of local anesthetics. In one study ($n = 56$) using lidocaine and varying amounts of clonidine, the duration and onset of anesthesia were improved for patients undergoing carpal tunnel release ($p < 0.01$) (Bernard & Macaire, 1997). A disadvantage of adding clonidine was an increased incidence of sedation and hypotension. In a study of sciatic nerves in mice ($n=40$), clonidine added to bupivacaine increased the duration but decreased the maximal anesthetic effect (Attolini, Gantenbein, Grignon, & Bruguerolle, 1995). With the availability of more potent and longer acting local anesthetics, the use of clonidine, which can cause sedation and hypotension, may not be in the best interest of the patient.

Researchers have examined the use of potassium channel agonists combined with local anesthetics (Gantenbein, Attolini, & Bruguerolle, 1996). Theoretically, the potassium channel agonist should hyperpolarize the cell membrane, further slowing the propagation of the action potential. In one study, different potassium channel agonists increased the duration of bupivacaine but the maximal effects were mixed depending upon the agonist used (Gantenbein et al., 1996). This study was done in a laboratory on sciatic nerves of 170 mice. The potassium channel agonists were injected in the intraperitoneal space exclusively, and local effects were not assessed.

Side Effects.

Side effects of local anesthetics may include pain, hematoma, tissue necrosis, poor wound healing, and neurotoxicity. Allergic reactions manifest as rash, urticaria, laryngeal edema, bronchospasm, and hypotension (Stoelting, 1995). Allergic reactions are extremely rare but have been reported (Brown, Redden, & Chan, 1995). Ester type local

anesthetics that produce metabolites related to para-aminobenzoic acid are more likely to evoke an allergic reaction. Preservatives, such as methylparaben, have a similar chemical structure to para-aminobenzoic acid and are used in commercial preparations of ester and amide local anesthetics. These preservatives may also evoke allergic reactions (Stoelting, 1995). Patients who have a history of multiple allergies are more susceptible.

Accidental intravascular injection of local anesthetics during the performance of peripheral nerve blocks can produce excess plasma concentrations of the local anesthetic leading to systemic toxicity. Early systemic effects may include tingling sensations, tinnitus, metallic taste, nervousness, and slurred speech (Dennison et al., 1995; Skidmore et al., 1996). Severe systemic reactions are rare but start with convulsions, progressing to hypotension, leading to apnea, and finally circulatory collapse (Santos et al., 1995). In one study (Santos et al., 1995), 48 ewes were given continuous infusions of either ropivacaine or bupivacaine until they died. The pattern of toxicity was the same in all but two ewes in the bupivacaine group. These two ewes progressed from convulsions to circulatory collapse within one minute.

Bupivacaine has been suggested to be more cardiac depressing than other local anesthetics because of its longer duration of action on sodium channels in the heart (Veering, 1996). Freysz et al. (1995) found that bupivacaine prolonged conduction time and decreased the fibrillation threshold significantly in pigs ($p < 0.05$). The researchers attempted to control extraneous variables such as temperature and heart rate, which can lead to fibrillation. Ischemia to the heart was produced by occlusion of a major coronary artery mimicking a possible clinical occurrence. The results of this study are supported by a similar bupivacaine study by Moller and Covino (1993). In vitro rabbit hearts ($n = 42$) had prolonged ventricular conduction time ($p < 0.001$). Furthermore, ventricular

fibrillation was noted even at low bupivacaine concentrations.

Ropivacaine was developed to be a less cardiotoxic replacement for bupivacaine while maintaining a long duration of action. Research has not supported ropivacaine as a suitable substitute. Santos et al. (1995) compared the systemic toxicity of ropivacaine and bupivacaine. In non-pregnant ewes, toxic doses of these drugs were not significantly different ($p < 0.05$). In pregnant ewes, lower doses of bupivacaine caused toxicity. The authors attributed the low toxic dose of bupivacaine in pregnant ewes to lower protein binding during pregnancy and the longer elimination rate of bupivacaine. These results were obtained on laboratory animals using continuous intravenous infusions. The results cannot be directly extrapolated to the clinical environment; however, the results can serve as a guide for choosing the drug and for assessing inadvertent intravenous injection.

Overall, local anesthetics have been shown to give rise to low morbidity and mortality rates. In the United Kingdom, Dennison et al. (1995) conducted a twelve year retrospective study of patients who received lidocaine, bupivacaine, or prilocaine via local infiltration ($n = 116$). These investigators found no morbidity or mortality related to local anesthetics. The amide local anesthetics studied were administered in doses less than 80% of the maximal recommendations.

Opioids

The term opioid is used to designate a group of drugs that are opium or morphine like. Opium was extracted in an impure form from the juice of the poppy seed. Originally, opioids only included the different extracts from opium such as morphine and codeine. As technology advanced, the opioid drug classification broadened to include synthetic derivatives that have agonist or antagonist morphine-like action. Opioids share some of the properties of three neuropeptides families: the enkephalins, endorphins, and

dynorphins. These neuropeptides are known as endogenous opioids (Reisine & Pasternak, 1996). For the purpose of this paper, an opioid is any substance, exogenous or endogenous, with a mechanism of action at an opioid receptor.

Mechanism of Action of Opioids

There is evidence for three major classes of opioid receptors: mu, kappa, and delta. There are several subtypes for each class. All of the subtypes modulate pain perception, with the exception of the type-two kappa (K_2) receptor, which has not been adequately examined (Dhawan, et al., 1996; Minami, & Satoh, 1995; Pasternak, 1993; Thorpe, 1984). Reisine and Pasternak (1996) described the mechanism of action of the opioid receptors as via activation of pertussin toxin-sensitive guanosine 5-triphosphate (GTP)-binding proteins. Activation of these proteins, as would occur with an opioid, leads to one or more distinct pathways. The first pathway is inhibition of adenylyl cyclase activity. When this occurs, phosphorylation of various intracellular proteins is inhibited. This prevents the neuron from releasing its neurotransmitter. A second pathway is the activation of ligand-operated potassium channels leading to hyperpolarization of the neuron membrane. This hyperpolarized neuron does not release its neurotransmitter and the action potential is not propagated. Finally, activation of the GTP-binding proteins may inhibit the activation of voltage-gated calcium channels. When these channels are inhibited, depolarization of the cell membrane does not occur. Reisine and Pasternak stated that the calcium or potassium mechanism is the most feasible explanation for opioid blockade of pain transmission.

Animal studies exist that evaluated the effect of adding opioids to peripheral nerve tissue. In general, these studies involved the injection of selective opioid receptor agonists into inflamed and noninflamed peripheral nerve tissue. Stein et al., (1988) found

the application of opioid receptor agonists into inflamed rat hind paws increased the pressure required to elicit paw withdrawal. To confirm that enhanced pain tolerance was the result of opioid receptor activation, the researchers injected selective opioid receptor antagonists into the paw. It was noted that the pressure required to produce paw withdrawal was reduced to baseline levels. These results support the theory that there are functional opioid receptors in peripheral nerve tissue. Other studies have produced similar results (Gissen, Gugino, Datta, Miller, & Covino, 1987; Joris et al., 1987; Stein, 1993).

In vitro experiments conducted by Armstrong, Power, and Wildsmith (1991) on isolated desheathed rabbit nerve preparations have shown that fentanyl has local anesthetic actions. Fentanyl also augmented the effects of bupivacaine. These results have not been replicated on human nerve fibers. Some opioids may have non-receptor, axonally mediated, local anesthetic effects on peripheral nerves (Gissen et al., 1987). Opioids injected into a nerve sheath may either diffuse proximally or be transported to the substantia gelatinosa, where opioid receptors are known to have effects on nociception (Cousins et al., 1988). The most likely mechanism of action for the peripheral effects of opioids is the existence of opioid receptors in the peripheral tissues.

Side Effects of Opioids

The addition of opioids to regional techniques, such as subarachnoid anesthesia and epidurals, has gained widespread acceptance. Unfortunately, the problem of central side effects remains a concern (Cousins et al., 1988). An important goal of using opioids peripherally is the elimination of central side effects. Central side effects of opioids include, but are not limited to pruritis, vomiting, respiratory depression, and urinary retention (Cousins, & Mather, 1984). These side effects can occur with the administration

of opioids orally, intravenously, or spinally. Smaller doses administered perineurally may decrease these effects.

The incidence of side effects in intrathecal opioid administration is much higher than with peripheral opioid administration. Bozkurt, Kaya, and Yeker (1997) collected data on the side effects experienced by 175 children who received epidural opioids. Of the 175 subjects, 1.1% developed respiratory depression, 34% had nausea, 42.9% had vomiting, and 82% required urinary bladder catheterization. In this study, it was not clear if the side effects were due to the opioid, epidural, pain, or other confounding variables. In another study of adult subjects, investigators found that pruritis was the major side effect of opioids in spinal anesthesia (Liu et al., 1995).

In a study conducted with morphine administered peripherally in the brachial plexus (Flory, Van-Gessel, Donald, Hoffmeyer, & Gamulin, 1995), investigators found that the most common central side effects were nausea, vomiting, and pruritis. However, patients in both the experimental and control groups experienced side effects. Nausea and vomiting occurred in 15 of the patients ($\underline{n} = 40$). Ten of these patients were in the experimental group and five were in the placebo group. Pruritis occurred in three patients, all belonging to the placebo group. In another study in which morphine was administered peripherally for chronic pain ($\underline{n} = 25$), researchers reported no subjective or objective central effects related to morphine (Mays et al., 1987).

Addition of Opioids to Local Anesthetics

The use of local anesthetics for regional anesthesia has been shown to provide effective anesthesia with minimal side effects. In addition, peripheral opioids have fewer side effects than systemic opioids. Theoretically, combining local anesthetics with opioids in the brachial plexus should produce synergistic effects. This should improve the

duration of postoperative pain relief with minimal side effects.

Studies that Do Not Support the Addition of Opioids to Local Anesthetics

In several studies on perineurally administered opioids, researchers found either no improved effect or an improved effect that was not clinically significant. Fletcher, Kuhlman, and Samii (1994) reported no improved analgesia ($p > .05$) after adding 100 mcg of fentanyl to 38 ml of 1.5% lidocaine ($n=53$). The researchers assessed the onset and duration of anesthesia, but did not assess pain. Kardash et al. (1995) conducted a similar study using 75 mcg of fentanyl added to 30 ml of 1.5% mepivacaine for brachial plexus anesthesia. In this study, the mean visual analogue scale (VAS) score was significantly decreased ($p = 0.039$) in the fentanyl group one hour postoperatively. Postoperative analgesic requirements and pain scores were similar between the groups during the next 12 hour postoperative period. Therefore, the authors of this study did not consider the lower mean VAS score one hour postoperatively to be clinically significant. The investigators monitored blood levels of fentanyl to rule out systemic effects. Racz et al. (1991) compared 5 mg of intravenous morphine with 5 mg of perineural morphine plus bupivacaine. From the results of this study, the researchers suggested that there is no difference in onset, quality, or duration of anesthesia. A probability value of less than 0.05 was considered significant by the authors. No specific level of significance was given. There was no difference in postoperative pain between the groups. It is possible that the use of bupivacaine, which is a long acting local anesthetic, masked the effects of the morphine. Flory et al. (1995) added morphine to bupivacaine in a brachial plexus anesthetic. The effect of the anesthetic and the analgesic requirements of patients during the first 48-hours following surgery were not different.

Studies that Support the Addition of Opioids to Local Anesthetics

Clinical trials provide evidence that the addition of an opioid to peripheral nerve tissue improves postoperative pain relief. Bourke and Furman (1993) demonstrated that there was improved postoperative analgesia when morphine was added to a 1.5% lidocaine with 1:200,000 epinephrine axillary anesthetic solution ($n = 40$). Although statistical significance was not reached, the investigators concluded that there was a clinically significant decrease in the number of postoperative supplemental analgesic capsules consumed by the experimental group. The researchers monitored the quality of pain using a Visual Analog Scale (VAS). Additionally, the amount of supplementary analgesia required by the patients over the first 24 hours postoperatively was also assessed. The researchers concluded that the addition of morphine provided an analgesia sparing effect. The patients who received morphine in the axillary anesthetic solution had lower VAS scores and required only about half the amount of supplemental analgesics as the control group. Viel et al., (1989) demonstrated an improved analgesic effect with the addition of opioids to an axillary anesthetic. These investigators compared buprenorphine to morphine in supraclavicular nerve anesthesia ($n = 40$). Buprenorphine provided prolonged analgesia that lasted 35 hours while morphine provided 18 hours of additional analgesia ($p < 0.001$).

Summary

Further research on management in the postoperative patient will expand the anesthesia care provider's arsenal of treatment modalities available to treat and manage postoperative pain. Patients undergoing brachial plexus anesthesia for surgery of the upper extremity and shoulder may have improved postoperative pain control with morphine added to their block. If this enhanced postoperative pain control allows the

patient to have an improved post surgical experience, the health care organization would benefit through more efficient use of resources.

Following a review of the literature, the investigators concluded that examination of the effects of morphine added to brachial plexus anesthetic solutions was warranted. Current data addressing the effectiveness of the addition of morphine to local anesthetics at peripheral sites is equivocal. Some investigators have reported prolonged analgesia with the use of opioids added to the brachial plexus anesthetic solution (Bourke & Furman, 1993; Viel et al., 1989); other investigators have been unable to replicate these results (Kardash et al., 1995, Fletcher et al., 1994, Racz et al., 1991). The information gathered in this study added to this existing body of knowledge.

CHAPTER III

Methodology

The purpose of this study was to compare the onset of postoperative pain in subjects who received 75 mcg/kg of preservative free morphine and 1.5% mepivacaine with 1:200,000 epinephrine into the brachial plexus sheath to those who received 1.5% mepivacaine with 1:200,000 epinephrine into the brachial plexus sheath. The investigators used a prospective, randomized complete block, single-blinded design with manipulation of the anesthetic solution. This chapter includes a description of the population, setting, sample, protocol, instrumentation, data collection procedures, protection of human subjects, study design, and data analysis.

Population, Setting, and Sample

The population for this study was patients who presented for surgery of the shoulder and/or upper extremity at a large medical center in the Southeastern United States. This medical center received referrals from a 3-state region. The sample consisted of patients who were 18 years of age and older undergoing surgery to the shoulder, arm, forearm, and/or hand and had legal competence to give consent. Patients classified as American Society of Anesthesiologists (ASA) physical status I, II, III, or IV, to include emergency cases, were considered for this study. The ASA classification is used to designate patients into categories that provide a general guideline for anesthesia care providers to assess the probability of the patient experiencing anesthetic morbidity or mortality. Definitions for the ASA physical status classification system are included in Table 3. Excluded from this sample were patients with any absolute contraindication for brachial plexus anesthesia.

Table 3

ASA preoperative physical status classification system

Class	Definition
I	A healthy patient.
II	A patient with mild systemic disease and no functional limitations.
III	A patient with moderate to severe systemic disease with no resulting functional limitation.
IV	A patient with severe systemic disease that is incapacitating and a constant threat to life.
V	A moribund patient who is not expected to live 24 hours with or without surgery.
VI	A brain-dead patient whose organs are being harvested.
E	An emergency procedure is followed by "E" (for example, "II-E").

Patients with hypersensitivities to any of the study medications were also excluded. Patients classified as ASA V or VI were excluded from the study because their underlying medical condition would interfere with the patient's ability to give informed consent and the investigator's ability to collect data.

The investigators used convenience sampling. Convenience sampling is defined as the use of the most readily available individuals as study subjects (Polit & Hungler, 1995). The sample size was determined using a power analysis performed using the Statistical Package for the Social Sciences© module Sample Power Version 1.2 in accordance with Cohen's *f*, a method of standardizing effect size (Cohen, 1992). Investigators reviewed previous studies, consulted with anesthesia care providers, and consulted a statistician. Using the information gathered, the investigators predicted a mean delay of 7.6 hours to the onset of postoperative surgical pain for subjects in the experimental group. The predicted delay for the control group was 6.0 hours. A standard deviation (SD) of 2 hours was predicted for both groups. This means the standard difference (*d*) was calculated to be 0.80. According to Cohen, a *d* of 0.80 is a large effect size ($f = 0.40$). Using a four group, two-way design with a power of 80 ($1-\beta = 0.80$), a level of significance of 0.05 ($\alpha = 0.05$), and an large effect size of 0.40 ($f = 0.40$), it was determined that a sample size of 14 subjects for each study group ($n = 56$ total) would be required to display significance.

The power analysis was conducted using results obtained by previous researchers who investigated the effects of the addition of opioids to the brachial plexus sheath on postoperative pain relief. According to Bazin et al. (1997), the addition of 75 mcg/kg of morphine to a 1% lidocaine and 0.5% bupivacaine solution with 1:200,000 epinephrine provided a mean delay in the onset of postoperative pain of 21 hours, with a range of 9

to 27 hours. Racz, Gunning, Dalla Santa, and Forster (1991) found that the mean time until the onset of postoperative pain was 8 hours (± 42 minutes). Brachial plexus anesthesia was provided using 5 mg of preservative free morphine in a 1% lidocaine and 0.5% bupivacaine solution. Therefore, based on these studies it was determined that a large effect size was warranted.

Protocol

After obtaining informed consent, subjects were randomly assigned to either the experimental or control group using a random number generator. In this study, the paresthesia, transarterial, or nerve stimulator techniques were used to achieve the axillary block. For each technique, the subjects were placed in the supine position, and the operative arm was extended to a 90-degree angle with the elbow flexed. The anesthesia care provider located the axillary artery by palpation, using the coracobrachialis and triceps muscles as landmarks. After aseptic preparation, a skin wheal was raised using 1% lidocaine over the anticipated site of injection.

The local anesthetic solution for the control group consisted of 1.5 % mepivacaine with 1:200,000 epinephrine. For the experimental group, the local anesthetic solution was manipulated by adding 75 mcg/kg preservative free (PF) morphine. This dose of PF morphine was chosen due to its effectiveness in delaying the onset of postoperative pain as demonstrated by Bazin et al. (1997). A 2.5% solution of PF morphine was used for this study because its addition to the local anesthetic solution would not significantly contribute to the total volume of local anesthetic solution applied to the brachial plexus sheath. For example, a 70 kg subject required only 0.21 ml of 2.5% PF morphine solution. A maximum of 40 ml of local anesthetic solution was injected into the brachial plexus. Additional blocks were performed if deemed necessary by the anesthesia

care provider. These additional blocks included ring, coracobrachialis, or single nerves of the upper extremity. If additional blocks were performed, the volume of local anesthetic used for these blocks, usually 3-5 ml, was not be included in the maximum volume. Sites of injection and volume used for each block were documented on the Brachial Plexus Block Data Tool (Appendix A).

Intravenous access was established and standard patient care monitors (blood pressure cuff, pulse-oximeter, and electrocardiogram electrodes) were applied prior to the administration of the block. The anesthesia care provider determined the need for supplemental oxygen administration. When deemed necessary by the anesthesia care provider, patients received intravenous medication for adequate sedation, anxiolysis, and analgesia. Intravenous narcotics, excluding morphine, were administered intraoperatively if the patient required analgesia. The anesthesia care provider performed an axillary or combined general/interscalene technique for the brachial plexus anesthetic. General endotracheal anesthesia was the backup anesthetic plan for the axillary approach.

Two methods of administering an axillary anesthetic using the paresthesia technique were employed. One way was with the aid of a peripheral nerve stimulator. An insulated 22-gauge needle was connected to a peripheral nerve stimulator. The current was set at two milliamps, and the needle was directed toward the arterial pulse. The anesthesia care provider waited for a response to electrical stimulus of muscles innervated by the motor fibers of the radial, ulnar, median, and musculocutaneous nerves. The amperage was reduced to 0.5 milliamps or less while continuing to produce the desired motor response. At this point, a small amount of the local anesthetic solution was injected. Rapid cessation of the motor response confirmed appropriate needle placement. The remainder of the local anesthetic solution was injected in small increments while

aspirating for blood before each injection.

A second way to perform the paresthesia technique was by locating the arterial pulse and stabilizing the axillary artery with the index and middle fingers of the non-dominant hand. A 22-gauge short bevel needle (B-bevel needle) attached to a 30 milliliter syringe and connecting tubing with a three-way stopcock was advanced toward the arterial pulse. The needle was advanced until a paresthesia was elicited. The location of the paresthesia in the distal arm or fingers was used to determine the proper location for anesthetic solution injection. Prior to the injection of the local anesthetic solution, proper needle position within the brachial plexus sheath was confirmed by the absence of blood on aspiration. The local anesthetic solution was deposited into the brachial plexus sheath in three to five milliliter increments while aspirating for arterial blood. After completion of the block, pressure was applied distal to the injection site to promote central migration of the solution. If the artery was penetrated using a paresthesia technique, the anesthesia care provider documented this and attempted the paresthesia technique again, or converted to a transarterial technique.

The transarterial technique differed from the paresthesia approach in that the axillary artery was deliberately penetrated with the needle. While advancing the needle toward the axillary artery, continuous aspiration was performed. The anesthesia care provider assessed for the presence of arterial blood, which confirmed the location of the axillary artery. The needle was advanced through the axillary artery until blood was no longer aspirated. At this point, the needle was slightly posterior to the axillary artery. The local anesthetic solution was injected in three to five milliliter increments, while aspirating for blood between injections. The amount of local anesthetic solution injected

varied between anesthesia care providers. All of the local anesthetic solution was either injected posterior to the artery, or in divided doses between the posterior and anterior locations. After the injection posterior to the axillary artery was completed, the anesthesia care provider withdrew the needle slowly. When blood was no longer aspirated, the needle was anterior to the axillary artery. Digital pressure was applied distal to the injection site to facilitate the central spread of the local anesthetic solution.

For the axillary approach, a ring block was usually performed. This block provided anesthesia to the intercostobrachial and medial brachial cutaneous nerves. Small amounts (3-5 ml) of the local anesthetic solution were injected into subcutaneous tissue from the deltoid prominence to the most inferior aspect of the medial portion of the arm. Redirecting the needle into the body of the coracobrachialis muscle provided additional anesthesia. Three to five milliliters of the local anesthetic solution injected in a fanwise manner anesthetized the musculocutaneous nerve. The anesthesia care provider aspirated for the presence of blood prior to the injection of the local anesthetic solution.

The interscalene technique was performed with the subject supine and the head turned away from the side blocked. The sniffing position was used to identify the borders of the sternocleidomastoid muscle, anterior, and middle scalene muscles. The borders were marked with a pen. The interscalene groove and cricoid cartilages were palpated and used as landmarks. A 22-gauge insulated needle was inserted nearly perpendicular to the skin in a caudad and posterior direction. The needle was advanced until persistent paresthesias or muscle responses to stimulation of the motor nerves occurred in the distal arm or fingers. When a muscle response was observed, the voltage was reduced from 2 milliamps to the lowest possible amperage capable of sustaining the response (optimal of 0.5 milliamps but not less than 0.2 milliamps). The needle was fixed in this

position, and a maximum of 40 ml of local anesthetic solution was injected with intermittent aspiration for the presence of blood.

After completion of the surgical procedure, the subject was monitored according to the hospital's postanesthesia care guidelines. Standardized orders were written concerning interventions to address pain which was the variable being assessed. Orders for postoperative pain were written at the discretion of the anesthesia care provider. Pruritis, nausea and vomiting, and a decrease in respiratory rate were also followed and data concerning these events was documented per the study protocol. The medications used for treatment of these events was also documented. If necessary, intravenous meperidine was administered to control postoperative shivering in the PACU. The dose required to control shivering typically ranges from 12.5 to 50 mg. According to Coda (1997), analgesic doses of meperidine range from 0.1 to 1.0 mg/kg. To minimize the influence of meperidine on the patients' perception of pain, the minimum required dose to attenuate shivering was administered.

Instrumentation

After informed consent was obtained on all subjects, bright pink label was placed on the patient's chart identifying the subject as part of the study. Data collection began on the subject's day of surgery. Instrumentation for this study included the Brachial Plexus Block Data Tool, Sensory and Motor Assessment Tool, Telephone Survey Tool, and Modified Numeric Rating Scale.

Brachial Plexus Block Data Tool

The investigators developed the Brachial Plexus Block Data Tool (see Appendix A). This tool was used to gather information pertinent to the subject, surgical procedure, brachial plexus technique, and adjunct anesthetics. Other information documented on this

tool included a baseline pain assessment and unusual occurrences or side effects. The Brachial Plexus Block Data Tool was developed after information was gathered from a review of the literature, personal communication with anesthesia care providers, and consultation with a statistician.

Sensory and Motor Assessment Tool

The investigators combined an assessment procedure designed by Koscielniak-Nielsen, Christensen, Stens-Pedersen, and Brushoj (1995) and a numeric rating scale developed by Bromage (1976) to create the Sensory and Motor Assessment Tool (see Appendix B). This sensory and motor function assessment tool is used in anesthetic practice and is widely accepted by the anesthetic community (Bridenbaugh, 1988). In addition, the tool has been used extensively in research to evaluate sensory and motor function following brachial plexus anesthesia (Gormley et al., 1996; Hickey et al., 1991; Hickey et al., 1993; Hickey et al., 1992; Mackay & Bowden, 1997). The investigators of this study could not find specific references in which the reliability and validity of these procedures were tested.

The technique used to evaluate sensory innervation was the application of a sharp object (e.g., the end of a broken tongue blade) to the skin of the shoulder and/or upper extremity. The sharp stimulus was applied to the area of cutaneous innervation supplied by seven nerves: axillary (lateral side of upper arm), musculocutaneous (lateral side of forearm), radial (web space between thumb and index finger), median (thenar eminence), ulnar (little finger), medial cutaneous nerves of the arm (medial side of the upper arm), and forearm (medial side of the forearm). Response to cutaneous stimulation was documented using a 0 to 2 numeric rating scale (0 = no loss of sensation to pinprick, 1 = analgesia (patient feels touch but not pinprick), 2 = no sensation of touch).

The technique used to assess motor function consisted of evaluating the subject's ability to move the shoulder and upper extremity against gravity and/or applied resistance. The motor function of five nerves was assessed: ability to abduct shoulder (axillary), ability to flex the forearm (musculocutaneous), ability to extend the forearm (radial), ability to oppose the thumb and fifth finger (median), and ability to adduct and abduct the little finger (ulnar). Motor function was documented using a numeric rating scale (0 = no weakness, 1 = paresis, and 2 = paralysis).

In this study, the Sensory and Motor Assessment Tool was used to evaluate each nerve field for the return of sensory and motor function. This allowed for discrete evaluation of each type of nerve fiber. With this information, investigators determined if pain fibers were blocked longer than the fibers responsible for sensation and movement were blocked.

Telephone Survey Tool

The investigators developed the Telephone Survey Tool (see Appendix C). The purpose of this tool was to collect data on subjects who were discharged prior to the complaint of pain. The Telephone Survey Tool was used as a diary on which the subject's self reported time of onset of sensation, pain, and movement in the blocked extremity.

The Telephone Survey Teaching Tool (see Appendix D), developed by the investigators, was used to instruct subjects on the use of the Telephone Survey Tool. This was designed as a script from which the subjects were instructed to record information related to sensory and motor function, as well as pain. Researchers have demonstrated that patients can accurately recall and report postoperative pain (Mancuso & Charlson, 1995; Sisk, Grover & Steflik, 1991). In 1991, Sisk et al. reported that the pain the patient actually experienced in the hospital and what the patient remembered experiencing

correlated well ($n = 39$, $p < 0.001$). Pain recall was accurate from 5 months to greater than 3 years (Sisk, et al., 1991). The use of a diary facilitated the subjects' reporting of pain while decreasing the investigator's reliance on subject recall.

Telephone surveys have been used in nursing and other health related fields with good results (Cave, 1989; Edwards, Albullarade & Turnbull, 1996; Marcus & Crane, 1986; Nail, Greene, Jones & Flannery, 1989; Worth & Tierney, 1993). Telephonic contact with 116 patients who were discharged from a hospital in Cleveland, Ohio resulted in 39 % of these patients having pain management difficulties. The nurse making the telephone call was able to identify pain as a problem and intervene. These results support the need to be actively involved in patients' care after discharging them from the health care facility (Cave, 1989). Marcus and Crane (1986) described the use of memory aides on which the subject recorded events related to the objective of the survey. These aides helped reduce the amount of information given by the subject to open-ended questions and resulted in more discrete answers.

In this study, the Telephone Survey Tool allowed the investigators to collect data on discharged subjects. The majority of the sample had outpatient surgical procedures. Without the use of this tool, collection of data up to 24 hours post procedure would not have been possible.

Modified Numeric Rating Scale

The Modified Numeric Rating Scale is a method of evaluating pain intensity. This scale ranges from 0 to 10. Zero equals no pain, and 10 equals the worst pain ever experienced by the subject. In a study done in 1992, Scott concluded that a numerical scale for rating pain with verbal end points positioned next to the 0 and the 10 might be

the most effective tool for assessing acute pain levels. In a pilot study, Scott (1994) studied 40 patients and the nurses who cared for them. She used a pain assessment chart on which patients documented or had a nurse document their pain level on a scale from 0 to 10, with 0 anchored as "no pain" and 10 as "the worse pain I can imagine". Both the nurses and the patients found the tool easy to use and understand. Furthermore, patients found it easier to communicate their pain and felt they were given analgesia more readily.

Although there is more research available on pain assessment tools such as the 10 cm Visual Analog Scale (VAS) and the 0 to 5 point Numeric Rating Scale to support their validity and reliability, the investigators chose to use a Modified Numeric Rating Scale. The nursing staff at Dwight David Eisenhower Army Medical Center used this scale to evaluate pain. Keeping the same tool used by the nursing staff increased the reliability and validity of this tool.

Procedure for Data Collection

An investigator was assigned as the Investigator of the Week. The Investigator of the Week was responsible for facilitating the research for that week. A roster with the name and pager number for that investigator and an alternate was posted in each study folder and in all locations in which the subject received care. These locations included the operating room (OR), post anesthesia care unit (PACU), and ambulatory surgery center (ASC).

The surgical schedule was reviewed prior to the day of surgery for potential subjects. The Investigator of the Week approached each potential subject for participation in this study. Informed consent was obtained either during the preoperative interview or on the day of surgery. If the patient consent was obtained on the day of surgery, it was done so prior to the patient receiving any sedative medication. The assigned anesthesia

care provider completed the Brachial Plexus Block Data Tool on the day of surgery.

On the day of surgery, the Investigator of the Week ensured that the subject's chart was labeled with a bright pink tag. The anesthesia care provider obtained a preassembled study packet from the anesthesia workroom. This packet consisted of a yellow folder containing the data collection tools (see Appendices A, B, C, D, E, & F). The subject's identification number was placed in the upper right hand corner of each folder and on each data collection tool in the folder. On the inside flap of the folder was a card designating the subject as part of the experimental or control group. This packet remained with the chart throughout the subject's hospital stay. Upon discharge from the hospital, the Investigator of the Week collected the packet after completion of the discharge assessment. The Investigator of the Week reviewed the packet for completeness. The completed packets were stored in a locked cabinet in the anesthesia classroom.

The anesthesia care provider collected data concerning the subject's baseline pain status, the subject's demographics, the surgery, and the anesthetic technique. These data were documented on the Brachial Plexus Block Data Tool. This tool was completed prior to the subject's arrival in the PACU.

There were five scheduled data collection points in this study: preanesthetic; admission to the PACU; discharge from the PACU; discharge from the ASC/ward; and approximately 24 hours following the surgery. An additional data collection point occurred at the subject's first complaint of pain. At this point,data collection stopped. At each data collection point, the subject was assessed for the presence, intensity, and character of pain and for return of sensory and motor function.

The primary anesthesia care provider gathered the initial data. This data collection occurred during the preanesthetic assessment. Data concerning the subject demographics,

brachial plexus block technique, and the surgical procedure were collected. In addition, information concerning the subject's baseline pain and sensory and motor function was obtained prior to placement of the block.

The investigators collected data at all the subsequent data collection points whenever possible. PACU nurses were trained in the use of all assessment tools and were able to collect data in the event an investigator was unavailable. The nursing staff paged the investigator when receiving a study patient, at the subject's first complaint of pain, and upon discharge of the patient so that an investigator could perform the assessments on the subject.

The fifth data collection point occurred between 9:00 a.m. and 11:00 a.m. the day after surgery. If this time was inconvenient for the subject, an alternate time was agreed upon between the subject and the investigator. The subject was given the Telephone Survey Tool to take home. An investigator documented any sensory function, motor function, or pain the subject experienced. If sensory and/or motor function had not returned or the subject had not experienced pain by discharge, instructions were given for filling out these areas. Investigators called every subject regardless of whether or not that subject had experienced pain. This procedure increased the continuity of the study and gave a sense of closure to subjects. The follow up phone call was made by one of the investigators, using a prepared script to guide the data collection using the following procedure (see Appendix E). The investigator attempted to contact a subject twice the first day. If unsuccessful, the investigator called twice on the following two days. If the subject was not contacted by the third day, only the data obtained prior to discharge was used. An alternate investigator, not the provider who performed the anesthesia, made the follow up phone call for subject completion of the Telephone Survey Tool.

An additional data collection point occurred when the subject first reported pain. When a subject reported that he/she had pain, the nurse caring for that subject assessed the pain. Pain was evaluated for time of onset, intensity, location, and a description of the pain. At this time, the nurse paged an investigator who was responsible for performing a sensory and motor assessment on the patient. The results of these assessments were documented on the PACU/ASC/Ward Data Collection Worksheet (see Appendix F).

Evaluator Training

To increase the reliability of the data collection tools, as well as maximize staff involvement in the study, each anesthesia care provider and nurse involved in the study received instructions on the proper use of the data collection tools. The investigators conducted initial training sessions for the anesthesia, PACU, and ASC staff. New personnel to the PACU, ASC, and medical/surgical ward were identified by their head nurse and brought to the attention of the investigator of the week during the first week of each quarter. The investigator of the week conducted inservices for identified staff in need of training. Anesthesia and nursing staff were not involved in the research project until they had received this training.

Training sessions included instruction on completing the data collection tools and an explanation of the roles of each individual in the study. The anesthesia care providers received instructions on obtaining informed consent, completion of the Brachial Plexus Block Data Tool, the protocol and the medications used to perform the brachial plexus blocks. The PACU nurses received instructions on use of the Sensory and Motor Assessment Tool, completion of the PACU/ASC/Ward Data Collection Worksheet, and how to contact the Investigator of the Week. The investigators monitored the information recorded on the data collection tools for completeness. If necessary data were missing, a

subject's chart was used to complete the data collection tools. For example, patient demographics, anesthetic technique and medications used, and type and length of surgical procedure were obtained from the chart as needed.

The interrater reliability among the investigators was performed on the Sensory and Motor Assessment Tool prior to beginning data collection and on a quarterly basis. Initially, a Certified Registered Nurse Anesthetist (CRNA) taught the appropriate sensory and motor assessments. Each investigator was required to attend a class taught by this CRNA. Two investigators at a time assessed a mock subject. One investigator actually performed a sensory and motor function assessment of the mock subject. The second investigator observed and completed an additional sensory and motor assessment. Investigators obtained 100% agreement with the CRNA prior to their participation in the study. The Investigator of the Week performed quarterly interrater reliability testing on the Sensory and Motor Assessment Tool. Two investigators or an investigator and a PACU nurse independently assessed a subject using the Sensory and Motor Assessment Tool. The Investigator of the Week compared the two assessments. When there was less than a 90% agreement, the areas of disagreement were discussed and retraining was performed as needed. The investigators or PACU staff then independently rated another subject. Retraining and reassessments were performed until a 90% or better agreement was obtained. Documentation of each training session included date, time, reason for training, participants, and results of training. Training session documentation was kept with the study logbook in a locked cabinet in the anesthesia classroom. Investigators absent from the medical center and not involved in the study for greater than 4 weeks required retraining to a 90% interrater reliability prior to being involved in sensory and motor assessments. It was the responsibility of the returning investigator to schedule

retraining within the first week of returning to the medical center.

Protection of Human Subjects

Subjects who participated in this study incurred no risks above those associated with brachial plexus anesthesia. Written informed consent (see Appendix G) was obtained from the subject per guidelines published by the University of Texas-Houston Health Science Center (UT-HHSC) and the medical center at which the study was conducted. The potential subject was made aware that participation was voluntary and withdrawal from the study could occur at any time without consequence. All aspects of the study, to include benefits, alternatives, and risks, were discussed with each potential subject. The subject was informed that the results of this study would be disseminated in accordance with UT-HHSC guidelines and possibly submitted for publication in professional journals. The subjects were told that they would not be personally identified in any published report. A copy of the informed consent was placed in the subject's medical record.

Patient confidentiality was maintained by limiting access to identifying information. Personnel with access to study information included the anesthesia care provider, investigators, and faculty. All data collected was identified using subject identification numbers rather than names. Only the investigators had access to the document that linked the subjects' names to their numbers. This document was destroyed as soon as possible after data analysis was completed. The data collected in this study will be kept in a locked cabinet at the medical center for 5 years from the study completion. Investigators informed each subject that the investigators would provide a summary of the study results upon their written request.

Study Design

This was a quasi-experimental, prospective, single-blinded, 2x2 randomized complete block study design. Subjects were not randomly selected, but they were randomly assigned to the control or experimental group. Randomization was achieved using a random number-generating device developed by a statistician at the Medical College of Georgia. The control group consisted of subjects who received the local anesthetic solution without preservative free morphine. The experimental group consisted of subjects who received the local anesthetic solution with preservative free morphine. The anesthesia care provider mixed the local anesthetic solution. The technique used to administer the block was not randomized. The anesthesia care provider determined the appropriate brachial plexus anesthetic technique based on the type of surgery and the subject's input.

Procedural Pilot Study

A procedural pilot study was used to assess the protocol and to refine data collection procedures as needed. The first three subjects were considered pilot subjects. Since no major changes were made to the procedures following assessment of these subjects, they were included as part of the total study sample.

Potential threats to internal validity included selection bias, threat of instrumentation, and attrition. Use of the Brachial Plexus Block Data Tool allowed the investigators to monitor the demographic composition of each group. To minimize the threat of instrumentation, anesthesia care providers were given instructions on how to properly complete data collection tools. Discharge teaching about the Telephone Survey Tool was performed with the use of a script, which also decreased the threat of instrumentation. To minimize attrition, subjects were told to expect a follow up telephone

call between 9:00 – 11:00 am the day after their surgery. When the subject was not available at this time, further attempts to contact the subject continued for 72 hours.

Potential threats to external validity included: convenience sampling, experimenter effects, and the Hawthorne effect. Although it was necessary to use convenience sampling, subjects were randomly assigned to experimental and control groups. Comprehensive demographic data was collected to allow for a complete description of the study sample. Because this study was not double-blinded, a scripted explanation of the study and telephone survey was used. With the use of these scripts, investigators could not bias the sample by varying the way in which the instructions were given and questions were asked. This minimized the experimenter and Hawthorne effects.

Data Analysis

Data analysis was conducted with consultation from the Office of Biostatistics at the Medical College of Georgia. Subjects were placed into one of four groups based on the type of brachial plexus anesthesia received (axillary or interscalene) and local anesthetic solution administered (control or experimental). Analysis of Variance (ANOVA) was used to test the hypotheses. Using ANOVA and Fisher's Exact Test, the differences between the subjects within each group and the mean differences between the control and experimental groups were evaluated. If the differences between the groups were larger than the subject differences within the groups, it could be stated with confidence that the addition of preservative free morphine was responsible for the delay in onset of postoperative surgical pain. Descriptive statistics were used to describe the sample characteristics.

CHAPTER IV

Analysis of Data

In this chapter, the investigators discuss data and data analysis for this study in the following order: sample characteristics, primary findings and secondary findings. All data analysis was performed using SPSS© version 9.0 for Windows.

Sample Characteristics

Sample

The convenience sample was drawn from patients who received brachial plexus anesthesia using the interscalene or axillary approach at a regional medical center in the southeastern United States. A total of 29 patients participated in the study. The small sample size was due to various reasons. Of the 55 patients that met the criteria for participation in the study, 26 did not participate because of the following reasons. Six patients refused to allow the addition of morphine to the anesthetic solution. The reasons for refusal included fear of physical addiction to morphine, as well as side effects such as nausea/vomiting and pruritis. In such cases, the patient received either a general anesthetic, brachial plexus anesthetic without morphine, or local anesthetic with monitored anesthesia care.

Nine patients were not enrolled in the study because of their potential for conversion from an arthroscopic procedure to an open shoulder surgery. In these cases, the surgeon and anesthesia care provider agreed that bupivacaine would provide a much longer duration of postoperative analgesia than would mepivacaine, a local anesthetic of intermediate duration. These patients received a general anesthetic with or without a brachial plexus anesthetic solution containing bupivacaine. Five patients were not

brachial plexus anesthetic was more anesthesia than necessary for certain procedures of the wrist and/or hand. Examples of these procedures were hardware removal, fractured finger repair, or trigger finger release.

Pre-existing medical conditions accounted for the exclusion of four patients from the study. One patient was excluded due to nerve damage to the operative extremity. Another was excluded due to infection in the axilla at the time of surgery. One patient presenting for shoulder surgery had chronic obstructive pulmonary disease, a relative contraindication for an interscalene anesthetic (Bridenbaugh, 1988). One patient had a bipolar psychiatric disorder that impaired his ability to cooperate with the regional technique.

The final two patient exclusions were due to patient preference concerning participation in the study. One patient did not wish to invest the time required to complete the telephone survey tool. The other patient simply changed his mind about participation in the study for no particular reason.

Participant demographics for the 29 patients enrolled in the study are presented in Table 4. Demographics include age, gender, ethnicity, and ASA classification. Of the 29 subjects enrolled in the study, 4 of the subjects were removed from the study before the data collection end point. Three of these subjects, (1 female, 2 males), were from the axillary group. The fourth subject, a male, was from the interscalene group. All 4 subjects attritted prior to the start of surgery due to a failed block. A failed block was defined as subject movement and/or a subject's report of sensation in the surgical region. The two methods used to determine adequacy of regional anesthesia included a pinprick and Addison's test. The pinprick test, performed by the anesthesia care provider, involved the application of a sharp stimulus to the surgical site to assess sensory function. The

Table 4

Sample Characteristics for the Interscalene and Axillary Brachial Plexus Groups

Characteristics			Brachial Plexus Anesthetic Group			
			Interscalene (n = 12)		Axillary (n = 17)	
			Control	Treatment	Control	Treatment
	n	(%)				
Age						
18 – 34	15	(52)	5	4	2	4
35 – 49	10	(35)	1	1	5	3
50 – 64	1	(3)	0	0	1	0
65 – 79	3	(10)	0	1	1	1
Gender						
Male	21	(72)	5	5	6	5
Female	8	(28)	1	1	3	3
Ethnicity						
White	22	(76)	6	5	5	6
Hispanic	1	(3)	0	1	0	0
Black	6	(21)	0	0	4	2
ASA						
I	13	(45)	2	3	5	3
II	13	(45)	4	3	2	4
III	3	(10)	0	0	2	1

Note. % = Percent of total patient population Age = Age in years. ASA = American Society of Anesthesiologists physical classification.

Addison's test, performed by the surgeon, involved application of an Addison's forcep to the prospective surgical site to assess sensory function. If the block was determined to be inadequate, the surgical case was not cancelled, instead an alternate anesthetic procedure was provided. At this point data collection was terminated and the subject was attrited from the study. The n for this study's data analysis was 25.

Of the 25 subjects, 6 subjects were in the interscalene control group, 5 in the interscalene experimental group, 7 in the axillary control group, and 7 in the axillary experimental group. Male subjects were distributed evenly between the control, treatment, interscalene and axillary groups. Twenty-one males were enrolled in the study (72%), 11 of which were in the control group and 10 were in the experimental group. The interscalene group consisted of 10 males while the axillary group contained 11 male subjects. Females were distributed equally among the control and experimental groups, but not among the interscalene and axillary groups. There were three times as many females (75%) in the axillary group compared to the interscalene group (25%).

The ages of the subjects ranged from18 to 68 with a mean age of 40.72 years. It is of interest to note that 87% of the total patient population were between the ages of 18-49. The ethnic groups in this study's sample included 22 White (77%), 6 Black (20%), and 1 Hispanic (3%) subjects. The control and treatment groups in both approaches had an equal distribution of White subjects (11) in each group. All six Black subjects were in the axillary group and the one Hispanic subject was in the interscalene group.

The anesthesia care provider determined the ASA (American Society of Anesthesiologists) physical classification for each patient. There were no differences in subject representation between the control and treatment groups for each physical classification category. The majority (90%) of subjects was healthy ASA I/II patients.

The other subjects (10%) were ASA III. No subjects were classified as ASA IV or V.

All patients in the sample received orthopedic surgical procedures of the shoulder, arm, forearm, wrist, and hand. Table 5 lists the types of surgical procedures performed along with the type of regional technique used. The most common procedure performed using the axillary anesthetic approach was ganglion cyst removal (41%). Shoulder arthroscopic surgery (75%) was the most common type of procedure performed using the interscalene anesthetic approach.

Baseline Pain

Baseline pain was assessed following the collection of demographic data and is summarized in Table 6. Twenty-nine subjects participated in the pre-surgical baseline data collection point. The location and duration of the pain was assessed by subject report. In addition, the subject was asked to rate the pain on a 0-10 scale and provide a description of the pain. Eighteen (62%) subjects had baseline pain and 11 (38%) subjects did not. Of the 18 subjects that had baseline pain, 12 (67%) subjects had baseline pain for greater than one year, 6 (33%) subjects had baseline pain for less than one year. Subjects described their pain as dull/aching (50%), sharp/burning (44%), or tugging (6%). All nerve fields were represented in the description of baseline pain. Axillary and radial nerve fields were the most common sites reported for baseline pain.

Data Collection Points

Following the baseline pain assessment, there were four data collection points (DCP): admission to PACU (DCP#1); discharge from PACU (DCP#2); discharge from the ASC/medical-surgical ward (DCP#3); and the telephone survey (DCP#4). Data was also collected at the subject's first complaint of pain that may have occurred during the subject's recovery in the PACU (IPACU) or subsequently on the ward (IWARD). The

Table 5

Surgical Procedures on Study Subjects

Procedure	Brachial Plexus Anesthetic Group			
	Interscalene (n = 12)		Axillary (n = 17)	
	Control	Treatment	Control	Treatment
Ganglion Cyst Removal	0	0	2	5
Carpal Tunnel Release	0	0	0	1
Shoulder Arthroscopy	5	4	0	0
Open Shoulder Arthroscopy	1	0	0	0
Flexor Tendon Repair	0	0	0	1
ORIF Radial Fracture	0	0	1	1
Left Hand Fasciotomy	0	0	1	0
I & D of Hand	0	0	1	0
External Fixation of Wrist	0	0	0	1
AV Graft Placement	0	0	1	0
Thumb Ligament Recon.	0	0	1	0
Nirschel Procedure	1	0	0	0
CRPP	0	0	1	0
Elbow Scope	0	1	0	0

Note. ORIF = Open reduction and internal fixation. I & D = Incision and drainage. AV = Arterial to Venous. Recon. = Reconstruction. CRPP = Closed Reduction Percutaneous Pinning.

Table 6

Pain Character and Intensity at Data Collection Points

			Data Collection Points				
			#1	#2	#3		#4
Procedure	Approach	Base		IPACU	DPACU	IWARD	DWARD
Scope s.	ISB-C	d*4*			tu*5*	d*1*	
Open s.	ISB-C						
Scope s.	ISB-C	d*8*					d*5*
Nirschel	ISB-C	d*5*				d*5*	
Scope s.	ISB-C	s*8*		s*5*			
Open s.	ISB-C	s*9*				s*4*	
Open s.	ISB-T	s*4*				d*3*	
Scope s.	ISB-T				d*5*		
Scope s.	ISB-T			tb*7*			
Open s.	ISB-T	d*7*	ti*8*				
Scope s.	ISB-T	s*6*		s*7*			
CRPP	AX-C	d*4*					s*4*
GC	AX-C	s*6*					b*5*
ORIF r.	AX-C					s*2*	
Hand Fas.	AX-C						d*5*
I&D Hand	AX-C	d*2*			d*2*		
GC	AX-C						s*5*
GC	AX-C					d*6*	
AV Graft	AX-C			s*8*			
TLR	AX-C	s*10*		s*10*			
GC	AX-T	d*4*					
EFW	AX-T						s*5*
GC	AX-T						s*3*
FTR	AX-T	d*0*				d*4*	
GC	AX-T	s*0*					d

Note. IPACU = intra-pacu. DPACU = discharge pacu. IWARD = intra-ward. DWARD = discharge ward. Scope s. = shoulder scope. Open s. = open shoulder. CRPP = closed reduction percutaneous pinning. GC = ganglion cystectomy. ORIF r. = open reduction internal fixation radius. Hand Fas. = hand fasciotomy. I&D = incision and drainage. AV = arterial to venous. TLR = thumb ligament repair. EFW = external fixation wrist. FTR = flexor tendon repair. ISB-C = interscalene block control group. ISB-T = interscalene block treatment group. AX-C = axillary block control group. AX-T = axillary block treatment group. d = dull. s= sharp. ti = tingling. tb = throbbing. tu = tugging. Subjects that attrited are not included on table. Pain Intensity Scale: *0 – 10*; 0 = "no pain", *10* = "the worst pain one can imagine".

characteristics of pain reported by subjects at these data collection points are summarized in Table 6.

All 25 subjects participated in data collection in the PACU, which was the initial postoperative assessment for pain, sensory function, and motor function. At DCP#1, one subject reported pain. At DCP#2, three subjects reported pain. At DCP#3, one subject reported pain. Twelve subjects reported the onset of pain during their stay in the PACU (5) or the ward (7). Eight study subjects were discharged from the hospital pain free. At DCP#4, seven subjects reported pain. The researchers were not able to contact one subject who left the hospital pain free to determine the exact onset of pain. Sensory and motor function assessments were done on all subjects at the data collection points.

Primary Findings

This study was designed to determine whether the addition of 75 mcg/kg morphine to a local anesthetic solution for brachial plexus anesthesia would delay the onset of postoperative surgical pain. Hypothesis 1: The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, arm, and/or shoulder will delay the onset of postoperative surgical pain longer than a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

Power analysis was initially calculated for a large effect size. Power is the ability of the test to detect small but important findings, such as differences or associations (Polit & Hungler, 1995). The likelihood of detecting a difference (the power) is directly related to sample size. If the sample size is too small, it is not possible to show that anything is statistically significant. If the sample size is too large, then everything may be shown to be significant (Norman & Streiner, 1999). The power analysis indicated that a sample

of 56 subjects (14 in each group) would be sufficient for a large effect size. However, with the reduced sample obtained (n = 25), the effect size was moderate (power=0.31).

A two-factor analysis of variance (ANOVA) and Bonferoni multiple comparison test were used to determine the differences between the means of the four groups with regard to the time of onset of pain and the severity of pain. These groups included interscalene experimental, interscalene control, axillary experimental and axillary control. If the differences between the groups were larger than the subject differences within the groups, then it could be stated with confidence that the addition of preservative free morphine was responsible for the delay in onset of postoperative surgical pain.

Summary statistics for the ANOVA results are presented in Table 7. When the difference to onset of pain was analyzed based on treatment alone, there was no statistical difference between the control and experimental groups (p = 0.2792). When the data were analyzed with respect to approach by treatment, the interscalene control group had a mean of 5.56 hours, while the interscalene experimental group had a mean of 3.81 hours with a p of 0.1741. The axillary control group had a mean of 4.44 hours, while the axillary experimental group had a mean onset to pain of 7.65 hours with a p = 0.0106. These findings were statistically significant and hypothesis one was accepted for the axillary group.

The secondary hypothesis consisted of two parts corresponding to whether the addition of 75mcg/kg of morphine to a local anesthetic would alter the return of sensory and motor function. Secondary Hypothesis 1: The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, and/or shoulder will alter the return of sensory function when compared to a 1.5% mepivacaine with 1:200,000

Table 7

ANOVA Results for Time to Onset of Pain in Hours

Outcome	Variable	Range	Mean	SD	p-value
Time to Onset of Pain	Treatment				
	Morphine	1.9 - 13.9	5.73		0.2797
	No Morphine	2.5 - 8.3	4.89		
	Approach by Treatment				
	Interscalene – Morphine	2.5 - 4.8	3.81	0.94	0.1741
	Interscalene – No Morphine	3.1 - 8.3	5.56	1.87	
	Axillary – Morphine	1.9 - 13.9	7.65	3.73	0.0106
	Axillary – No Morphine	2.2 - 6.3	4.44	1.22	

Note. $p < 0.05$ is significant. Range and mean values represent hours.

epinephrine solution applied to the brachial plexus sheath prior to surgery.

Sensory function was assessed upon arrival to the PACU, discharge from the PACU, ASC, or the medical/surgical nursing ward, and at the first report of pain. The return of sensory function in seven nerve fields was recorded (axillary, median cutaneous of the arm, median cutaneous of the forearm, musculocutaneous, ulnar, median and , radial). Because the assessments occurred at specified events rather than specific time intervals, the exact onset of sensory function was not captured. The length of stay in the PACU ranged from 30 minutes to 150 minutes. The ASC/Ward length of stay ranged from 30 minutes to 270 minutes. Furthermore, the continuous assessment of motor and sensory function is not part of the PACU routine so data concerning sensory and motor function return could not be obtained as part of routine vital signs. Due to the inability to record the exact time of return of sensory function, the hypothesis can neither be accepted nor rejected.

Secondary Hypothesis 2: The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, and/or shoulder will alter the return of motor function when compared to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

Motor function was assessed upon arrival to the PACU, discharge from the PACU, ASC, or the medical/surgical-nursing ward, and at the first report of pain. Motor function may have returned prior to or after these times. The return of motor function in five nerve fields was recorded (axillary, musculocutaneous, ulnar, median and radial). The exact time of the return of motor function was not obtained in the data collection. Due to the

inability to record the exact time of return of motor function, the hypothesis can neither be accepted nor rejected.

Secondary Findings

Data was collected on the severity of postoperative surgical pain using the modified numeric rating scale 0 through 10, with 0 anchored as "no pain" and 10 as " the worse pain I can imagine". Although pain is a subjective phenomenon, this information was gathered because it allowed the investigators to quantitatively evaluate the characteristic of postoperative surgical pain at the onset. The modified numeric rating scale (NRS) can be used to measure both the intensity of acute pain and the efficacy of analgesic therapy (Flaherty, 1996). A two-factor ANOVA was used to analyze the difference concerning the mean severity of postoperative pain between the experimental and control groups for both the interscalene and axillary approaches to brachial plexus anesthesia (Table 8). There was no statistically significant difference ($p = 0.5530$) between the control and treatment groups concerning the severity at the onset of postoperative surgical pain. The mean severity of postoperative surgical pain for the control group was 4.70, and the mean severity for the treatment group was 5.11. The interscalene control group had a mean of 4.25, while the interscalene treatment group had a mean of 5.00. The axillary control group had a mean of 5.00, while the axillary treatment group had a mean of 4.60. These findings were not significant ($p=0.3097$).

The characteristic of postoperative surgical pain was also analyzed. The subjects were asked to describe the character of pain at onset. This description was matched with one of nine categories containing adjectives commonly used to describe pain (i.e. sharp, cutting, lacerating). Because the frequency of each group was less than five in some of the cells, the Fisher exact test was used to determine the difference in the

Table 8

ANOVA Results for Severity of Pain

Outcome	Variable	Range	Mean	SD	p-value
Severity of Pain	Treatment				0.5530
	Morphine	3.5 – 8.0	5.11		
	No Morphine	1.5 – 10.0	4.70		
	Approach by Treatment				0.3097
	Interscalene – Morphine	4.5 – 7.0	5.75	1.50	
	Interscalene – No Morphine	1.5 – 5.0	4.25	1.41	
	Axillary – Morphine	3.5 - 8.0	4.60	2.04	
	Axillary – No Morphine	2.0 – 10.0	5.00	2.69	

Note. $p < 0.01$ is significant. Range = 0 equals no pain and 10 equals the worst pain one can imagine. Mean = mean severity of postoperative surgical pain evaluated using the modified verbal descriptor scale.

characteristic of pain among the four groups at the time of onset of pain. The Fisher exact test is a nonparametric test that can be applied to nominal or ordinal data with sample sizes less than 30 (Polit & Hungler, 1995). There were no statistically significant differences in the characteristic of pain description at the time of onset between the control and treatment groups ($p = 0.859$). The two most frequently reported characteristics of postoperative pain were either a throbbing (46%) or sharp (42%) sensation followed by burning (8%) and tugging (4%). Summary statistics for the characteristics of postoperative surgical pain are presented in Table 9.

Data was also collected on all supplemental postoperative pain medications administered to study subjects. Figure 3 summarizes the type and frequency of analgesic administration to control and treatment subjects during the postoperative period while in the PACU, ASC/Ward, and Home. While in the PACU, one subject received Percocet, three subjects received Toradol, and four subjects received Morphine for pain. With regard to the ASC/Ward, three subjects received Demerol, two subjects received Percocet, one subject received Lortab, and one received Morphine for reported pain. At home, 13 subjects consumed Percocet, three consumed Lortab, and one consumed Motrin for postoperative pain. The investigators were unable to standardized postoperative analgesics due to surgeon and anesthesia care provider preference. In addition, the investigators were unable to convert the dosages of the various analgesics administered into equivalent potencies. For the above reasons, these data were not statistically analyzed.

In summary, it was found that the addition of PF morphine to a mepivacaine brachial plexus anesthetic solution did not provide statistically significant differences in the time to onset of postoperative surgical pain when the data were analyzed by treatment

Table 9

Fisher's Exact Test for differences between pain description at time of onset

Variable	Type of Pain				
	Sharp n (%)	Tugging n (%)	Burning n (%)	Throbbing n (%)	p-value
Morphine	3 (37.5)	0 (0.0)	1 (0.0)	5 (62.5)	0.859
No Morphine	7 (46.7)	1 (6.7)	1 (6.6)	6 (40.0)	
Axillary	7 (53.9)	0 (0.0)	1 (7.7)	5 (38.4)	0.377
Interscalene	3 (30.0)	1 (10.0)	1 (0.0)	6 (60.0)	
Axillary					0.862
Morphine	2 (50.0)	0 (0.0)	0 (0.0)	2 (50.0)	
No Morphine	5 (55.6)	0 (0.0)	1 (11.1)	3 (33.3)	
Interscalene					
Morphine	1 (25.0)	0 (0.0)	1 (0.0)	3 (75.0)	
No Morphine	2 (33.3)	1 (16.7)	0 (0.0)	3 (50.0)	

Note. $p < 0.01$ is significant. N = number of subjects.

(morphine versus no morphine). A statistically significant delay in the onset of postoperative surgical pain was demonstrated between the axillary experimental and control groups with the experimental group having a longer delay to the onset of pain. The return of sensory and motor function could not be statistically analyzed due to the inability to precisely record the onset times of motor or sensory functions. Secondary findings show no statistically significant difference in the severity or character of postoperative pain between the axillary and interscalene control and experimental groups and between the axillary and interscalene control and experimental groups concerning the amount of analgesics consumed in the hospital.

CHAPTER V

Discussion, Conclusions, Implications, and Recommendations

The use of opioids in regional anesthesia is not new; in fact opioids are routinely used in the subarachnoid and epidural spaces (Urmey, 1996). The discovery of opioid receptors in the peripheral nerve tissue has prompted exploration of the use of opioids in regional anesthesia (Kardash et al., 1995). Current data in which investigators addressed the effectiveness of the addition of morphine to local anesthetics at peripheral sites is equivocal. Some investigators have reported prolonged analgesia with the use of opioids added to the brachial plexus anesthetic solution (Bourke & Furman, 1993 & Viel et al., 1989) while other investigators have been unable to replicate these results (Kardash et al., 1995; Fletcher et al., 1994; & Racz et al., 1991). The purpose of this study was to compare the onset of postoperative surgical pain following surgery to the hand, forearm, arm, and/or shoulder in patients who received 75 mcg/kg preservative morphine combined with a 1.5% mepivacaine in 1:200,000 epinephrine solution to the brachial plexus sheath prior to surgery with patients who received a 1.5% mepivacaine and 1:200,000 epinephrine solution to the brachial plexus sheath prior to surgery. In this chapter, the investigators interpret findings as they relate to the research cited in the literature review. The hypotheses will be explained in light of the theoretical framework. The investigators will explore strengths and weaknesses of the research including limitations to the study. Finally, conclusions, implications for nursing, and recommendations for further research will be discussed.

Discussion

Hypothesis 1: The addition of 75 mcg/kg of preservative free morphine to a 1.5%

mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, arm, and/or shoulder will delay the onset of postoperative surgical pain longer than a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

There was no statistical difference in the onset of postoperative pain between the control and treatment groups with both approaches combined. When broken down by approach, there was statistical significance found in the time to onset of postoperative surgical pain between the control and experimental axillary approach group.

The mean time to the onset of postoperative surgical pain was 4.44 hours in the axillary control group and 7.65 hours in axillary experimental group. This was a 3.21 hour delay in the onset of postoperative pain. This is what the investigators expected to find. Based on the theoretical framework for this study, opioids should block the pain pathway. It is documented that opioids inhibit the calcium dependent release of excitatory, proinflammatory compounds (substance P) from peripheral sensory nerve endings (Stein, 1995). These findings are statistically significant ($p = 0.1369$) and are consistent with the theoretical framework.

The mean time to the onset of postoperative surgical pain was 5.56 hours in the interscalene control group and 3.81 hours in the interscalene experimental group. A p value of less than 0.01 was considered statistically significant. These results ($p = 0.1369$) were not statistically significant.

Discussion

The researchers expected to see a difference between the onset of pain between the different approaches to brachial plexus anesthesia. However, this was not the case. The axillary approach results indicate a delay in postoperative pain that is both statistically

and clinically significant. Whereas the interscalene approach group did not show a delay to the onset of postoperative pain. The most common surgical procedure performed for subjects in the axillary group was ganglion cyst removal (41%). According to Brody & Egan (1996), this type of surgical procedure is associated with minimal postoperative pain. Minimal pain combined with noninvasive procedures may explain the difference found between the axillary and interscalene approaches.

Several possible explanations for not finding a significant delay in the onset of postoperative surgical pain in the interscalene treatment group are a small sample size, data collection end point, and the use of supplemental blocks. A small sample size can make interpretation of results difficult. The sample size is related to effect size. Effect size is concerned with the strength of the relationship between variables. The more strongly the variables are interrelated, the smaller the sample size required to demonstrate a relationship between the variables (Polit & Hungler, 1995). The investigators believed that for this study, a larger sample size was necessary because the relationship between the variables is modest. In addition, pain is a variable that is difficult to quantify necessitating an even larger sample size to detect a difference between variables. The desired sample size for this study was 56 subjects with 14 subjects in the experimental and control groups for both approaches to brachial plexus anesthesia. The actual sample size of 25 subjects may have been too small to detect a difference between variables.

Another possible reason for the interscalene treatment group having a shorter time to the onset of postoperative surgical pain may have been related to the data collection end point. According to the study protocol, data collection stopped at the subject's first complaint of pain. Of the five interscalene experimental subjects, data collection on two subjects was stopped early because of a complaint of nonsurgical pain. In one subject,

data collection stopped after 2.5 hours due to a complaint of neck pain at the site of interscalene brachial plexus block injection. This subject denied pain at the surgical site but was medicated for the neck pain. Since pain was reported, the data collection endpoint was reached and data collection concerning the onset of pain was completed. The researchers were unable to reach this patient by telephone to determine the onset of surgical pain, but we believe that it would have been inaccurate because of the previous use of analgesics. The second subject in whom data collection stopped early complained of an "ache". This subject rated the ache as a three on the "0-10" numeric rating scale and refused pain medication. The first time the subject took pain medication was 21 hours and 25 minutes after the brachial plexus block.

The use of a supplemental block in an interscalene control group subject may have prolonged the onset of pain and thus provide another possible explanation for not finding a significant delay in the onset of postoperative surgical pain in the experimental group. This block contained 30 ml of 2% lidocaine and 0.5% bupivacaine in a 1:1 mixture. Bupivicaine has a duration of action of 240 to 480 minutes (Stoelting, 1995). Mepivacaine, with a duration of action of 60 to120 minutes, was the local anesthetic used in the study. The use of bupivacaine in the supplemental block may have prolonged the onset of postoperative surgical pain in this interscalene control subject.

Comparison to Current Literature

The results of this study are consistent with several previous clinical investigations that demonstrated the benefits of adding an opioid to a brachial plexus anesthetic solution. Viel et al., (1989) demonstrated an improved analgesic effect with the addition of opioids to an axillary anesthetic. These investigators compared buprenorphine (3mcg/kg) to morphine (50mcg/kg) in supraclavicular nerve anesthesia ($\underline{n} = 40$). Using a

three-point self-evaluation scale (1 = good or very good analgesia, 2 = tolerable pain, 3 = unsatisfactory or no analgesia), the investigators demonstrated that buprenorphine provided prolonged analgesia that lasted 35 hours while morphine provided 18 hours of additional analgesia ($p < 0.001$). This significant delay in the onset of postoperative surgical pain in the treatment group was not found in the results of our study.

In contrast, Fletcher et al. (1994) assessed the onset and duration of anesthesia after adding 100 mcg of fentanyl to 38 ml of 1.5% lidocaine ($n=53$) used for brachial plexus anesthesia. The treatment group did not experience a longer duration of postoperative analgesia than the control group ($p > 0.005$). Flory et al. (1995) added 5 milligrams of morphine to a 0.5% bupivacaine solution used for interscalene brachial plexus anesthesia. The effect of the anesthetic and the analgesic requirements of patients during the first 48-hours following surgery were not significantly different ($p > 0.05$). This was evidenced by a mean time to first analgesic intervention in the control group of 742 minutes while the treatment group had a mean time of 772 minutes.

Secondary hypothesis 1: The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, arm, and/or shoulder will alter the return of sensory function when compared to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

Secondary hypotheses 2: The addition of 75 mcg/kg of preservative free morphine to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery of the hand, forearm, arm, and/or shoulder will alter the return of motor function when compared to a 1.5% mepivacaine with 1:200,000 epinephrine solution applied to the brachial plexus sheath prior to surgery.

Due to the inability to record the exact time of return of sensory and motor function, the above hypotheses can neither be accepted nor rejected.

Discussion

It is generally thought that motor function will return before sensory function (Bridenbaugh, 1988). The investigators hypothesized that opioids would delay the onset of postoperative surgical pain for an undetermined period of time following the return of first motor function and then sensory function. The investigators' intent was to use the sensory and motor function data to support the primary hypothesis. There were five scheduled data collection points at which sensory and motor functions were assessed. These points were preanesthetic, admission to the PACU, discharge from the PACU, discharge from the ASC/ward, and the day after surgery. An additional data collection point occurred at the subject's first complaint of pain. The use of events rather than specific time intervals during the subject's recovery limited the ability to capture the exact time that sensory and motor function returned.

Although exact time to the return of sensory and motor function was not measured, sensory and motor functions were assessed at frequent enough intervals to note a pattern. In all subjects, there was at least partial return of sensory and motor function at the time of onset of postsurgical pain. However, pain did not always occur with return of sensory and motor function. In three subjects, two subjects in the axillary experimental group and one subject in the interscalene experimental group, there was return of sensory and motor function with no pain reported by the subject. There was a delay to the onset of pain in these subjects ranging from 1 hour 23 minutes to 10 hours and 35 minutes from the point that it was recorded that sensory and motor function had returned. The times recorded for return of sensory and motor function return are based on scheduled assessment points, not

actual times, therefore the return of sensory and motor function may have actually returned at an earlier time.

All subjects had return of both sensory and motor function at discharge from the hospital, as assessed by either a 0 or 1 in all nerve fields, with the exception of one subject. This subject, from the interscalene control group, had no return of sensory or motor function in any nerve field at the time of discharge from the hospital. A possible explanation for this finding could be the administration of a supplemental block. This subject received 30 cc of 2% lidocaine with 0.5% bupivacaine mix as a 1:1 mixture, by the surgeon, at the incision site prior to the end of the procedure. The addition of such a solution to the surgical site provided a longer duration of anesthesia (120-240 minutes) than 1.5% mepivacaine with 1:200,000 epinephrine. The use of supplemental blocks after the interscalene approach in brachial plexus anesthesia is not unusual because the average success rate for this approach is 75% (Schroeder et al., 1996).

Another observation gained from using the Sensory and Motor Assessment Tool was the pattern of return of sensory and motor function. In the interscalene group, the ulnar nerve field was the first to return, followed by the median nerve field. In the axillary group, the subjects demonstrated a different pattern of sensory and motor return. The axillary nerve field, followed by the medial antebrachial cutaneous (median cutaneous of the forearm), and the musculocutaneous nerve fields, were the first to return. A reasonable explanation for this may be that the interscalene approach more reliably anesthetizes the axillary nerve fields and the axillary approach more reliably anesthetizes the ulnar nerve fields (Urmey, 1996).

Understanding the anatomy of the brachial plexus can further explain these findings. According to Mulroy (1997), the administration of an interscalene block may

provide inadequate anesthesia to the lowest branches of the brachial plexus. These branches are formed from nerve fibers originating from C8 and T1, which supply innervation to the distal (ulnar) border of the forearm. This anatomical configuration may explain the early return of sensory and motor function to the ulnar nerve field when compared to the other nerve fields.

The axillary approach frequently spares the medial, antebrachial cutaneous, and musculocutaneous nerve fields (Mulroy, 1997). This occurrence is due to the departure of these nerves from the brachial plexus sheath high in the axilla. Additional anesthesia to these nerve fields is routinely provided with the use of ring blocks. These supplemental blocks may not provide adequate anesthesia. This may explain the early return of sensory and motor function to the medial antebrachial cutaneous and musculocutaneous nerve fields when compared to the other nerve field distributions.

Additional Findings

In addition to the primary and secondary hypotheses, the investigators evaluated the differences in the severity of postoperative pain. No statistically significant differences were found in the intensity of pain between the treatment and control groups for both the interscalene and axillary approaches. The mean severity of pain ranged from 4.25 to 5.75 using the 0-10 numeric rating scale. At the onset of postoperative surgical pain, the subjects experienced a moderate (4 to 6) amount of pain. According to Bloomstone and Borsook (1998), a pain value of less than five is generally considered acceptable.

When the severity of pain was broken down by demographics based on ethnicity and gender there were some differences in the severity of pain. The majority of the sample was white (76%) males (76%) with a mean severity of pain of 4.9. Blacks (3 males and 2 females) had a mean pain severity rated as 5.2 which was consistent with the

mean pain score for the aggregate sample. The one Hispanic had a score of 7.0. This is above the mean pain score for all subjects. Bates et al. (1993) studied ethnocultural pain experiences in 372 patients and found that Hispanics were more expressive about their pain. Females in this study had a mean severity of pain of 7.0 on a 0-10 numeric rating scale. Raftery et al., (1995) reported that female patients seen in the emergency department described more pain than male patients ($p<0.01$, $n=190$). DePalma and Weisse (1997) pointed out that in most studies there was a tendency for females to report higher levels of pain than their male counterparts when all subjects were administered the same painful stimuli in a laboratory setting. The conceptual framework for this study depicts demographics as having an impact on pain and the data supports this.

Data pertaining to the character of pain was also collected. Prior to surgery, the baseline pain experienced by the subjects was most often described as dull and aching. It is interesting to note that pain described in these terms is usually associated with visceral pain due to tissue injury or compression (Bloomstone & Borsook, 1998). Postoperative pain experienced by the subject was most often described as sharp and throbbing. This description of pain is usually associated with somatic pain due to tissue injury such as postoperative pain (Bloomstone & Borsook, 1998). The data collected on the character of pain supports the investigators' assumption that the pain measured was post surgical pain. The investigators noted no pattern between the presence of baseline pain, the character on postoperative pain, and medication usage.

The investigators also collected data on the type and amount of medication administered postoperatively. One reason for collecting this data was to determine if the subject was treated for any of the common side effects associated with morphine. These side effects include nausea and vomiting. Aside from the morphine placed into the

brachial plexus sheath in the treatment group study subjects, no morphine was administered to any of the study subjects during the intraoperative period. Metoclopramide, ondansetron, droperiodol, and promethazine were administered for postoperative nausea. These medications, based on their mechanisms of action, may have caused sedation, which could have interfered with data collection. Metaclopramide and ondansetron have no sedative activity (Donnelly, Cunningham, & Baughman, 1999). Droperidol works at subcortical levels causing sedation and promethazine works in the brain stem reticular system where it causes sedation (Donnelly et al., 1999). The sedative effects of droperidol and promethazine may have influenced the subject's perception of pain or interfered with the data collection. Two subjects took either droperidol or promethazine for complaints of postoperative nausea. It was not possible to delineate if nausea was a side effect of specific anesthetic medications administered during the intraoperative period. The investigators did not see any apparent effects of these drugs on the data collected.

An additional reason for collecting data on postoperative pain medication was to add to the data collected concerning the onset of pain. Pain for which a subject requested medication would be assumed to be more intense than pain for which medication was not requested. Morphine, Demerol, Toradol, and Percocet were given for postoperative pain in the PACU and ASC. These drugs were prescribed at variable dosages and intervals, which was left to the discretion of the nurse. The amount or type of postoperative pain medications was not standardized by the study protocol, therefore, the researchers did not statistically analyze these data.

With regard to analgesic consumption during the postoperative period, one control subject consumed Percocet in the PACU and two control subjects were administered

Percocet on the ASC/Ward. Seven control and 6 experimental subjects consumed Percocet at home. Three subjects (1 control and 2 experimental) received Toradol and four subjects (2 control and 2 experimental) received morphine in the PACU. Morphine was also administered to one control subject on the ASC/Ward. One subject in the control group received Lortab on the ASC/Ward, and three subjects (1 control and 2 experimental) consumed Lortab at home. One subject in the experimental group consumed Motrin at home. It is interesting to note that only control subjects consumed analgesics on the ASC/Ward.

The surgeon prescribed Percocet, Lortab, and Motrin for postoperative pain experienced at home. The investigators did not standardize discharge pain medication. Furthermore, data collection was terminated with onset of pain, which occurred in 16 patients prior to discharge from the hospital. While some of these subjects were contacted telephonically as follow-up, data on postoperative pain medication consumption was not collected on all. Only seven subjects did not experience pain while still in the hospital. These patients were contacted via the telephone the following day. Six subjects were in the axillary group (3 treatment/3 control), with the remaining subject in the interscalene control group. Four of the subjects discharged without pain had a ganglion cystectomy performed, a minimally invasive procedure involving nominal postoperative pain (Brody & Eagen, 1996). With regard to this subset of patients, analgesics to include Motrin, Percocet, and Lortab were consumed at home with the onset of pain.

Conceptual Framework

The conceptual framework for this study was derived from the science of physiology and pharmacology. This theoretical framework provided direction for the

analysis of the interrelated concepts that comprised this study. The concepts included surgery, brachial plexus anesthesia, postoperative pain, and demographics (Figure 1). The conceptual framework depicted a delay in time to the onset of pain following a surgical event when morphine (opioid) was administered into the brachial plexus along with mepivacaine (local anesthetic). Statistically, the data analysis supported the conceptual framework for the axillary approach to brachial plexus anesthesia, with an additional 3.21 hour delay in the time to onset of pain in the axillary experimental group, but not for the interscalene approach to brachial plexus anesthesia.

This significance is consistent with a similar study cited in the literature review. Viel et al., (1989) demonstrated an improved analgesic effect with the addition of opioids to an axillary anesthetic. These investigators compared buprenorphine (3mcg/kg) to morphine (50mcg/kg) in supraclavicular nerve anesthesia ($n = 40$). The investigators demonstrated that buprenorphine provided prolonged analgesia that lasted 35 hours while morphine provided 18 hours of additional analgesia ($p < 0.001$). Bourke and Furman (1993) demonstrated that there was improved postoperative analgesia when morphine (0.1 mg/kg) was added to a 1.5% lidocaine with 1:200,000 epinephrine axillary anesthetic solution ($n = 40$). Although statistical significance was not reached, those investigators concluded that there was a clinically significant decrease in the number of postoperative supplemental analgesic capsules consumed by the experimental group.

Study Strengths

There were several strengths of this research study. The study was done using a quasi-experimental design with manipulation of the independent variable and the use of a control group. Randomization was not used for the approach to the brachial plexus anesthetic. Subjects were randomized into experimental and control groups.

The results of this study support existing literature regarding use of opioids in the brachial plexus. As with existing literature, the results of this study are equivocal with a significant difference found in the onset of pain in the axillary experimental group, but not in the interscalene experimental group. In this respect, this study contributes to the existing body of knowledge in this area of research.

Study Limitations

Several weaknesses of the study were identified which should be considered when interpreting these data. These considerations include sample size, recruitment, and the use of a convenience sample. Additional weaknesses were inability to randomize brachial plexus block approach, data collection on sensory and motor function, definition of pain, supplemental block usage, and extraneous variables.

The use of convenience sampling limits the generalizabiltiy of the results to all populations. The sample in this study primarily represents healthy white males. Because of the small sample size ($n = 29$), statistical significance may have existed, but may not have been detected. Pain, as a homogeneous entity, may require a very large sample to detect a difference.

The investigators were not able to randomize the approach to the brachial plexus anesthesia. The anesthesia care provider determined the approach. Because of the lack of randomization, subject demographics were not equally represented between the approach groups.

Several other extraneous variables may have impacted the results. The length of and time each subject spent in the PACU and ASC was, in part, dependent on the type of surgical procedure. To minimize these variables, the investigators collected data on the type of surgery performed and the onset of postsurgical pain was measured from the end

of the brachial plexus solution injection. Additionally, data collection points were structured according to the subject's flow through the PACU and ASC, rather than at preset times after the surgical procedure.

Due to a limited number of data collection points the exact time of return of sensory and motor functions was not captured. Data was collected only upon arrival to the PACU, discharge from the PACU, ASC, or medical/surgical ward, and upon the first report of pain. Sensory and motor functions may have returned prior to or after these times.

According to the study protocol, data collection stopped at the subject's first complaint of pain. Two of the five interscalene treatment subjects' data collection stopped due to a complaint that may not have been postsurgical pain. One subject had pain at the brachial plexus injection site and the other subject had an "ache" for which the subject required no pain medications. These two subjects may have skewed the results of this study with its small sample size. A more specific operational definition of pain would have captured this more accurately.

Another extraneous variable was the use of supplemental blocks by the surgeon. Bupivacaine was used in two subjects for supplemental blocks. This local anesthetic has a longer duration of action than mepivacaine, which was used in the study. The use of supplemental blocks by the surgeon may have prolonged the onset of postoperative surgical pain in these subjects.

The use of postoperative medications for nausea and vomiting was another variable not controlled for in this study. The medications which were administered in the PACU, ASC, and/or medical /surgical ward for nausea and vomiting included metoclopramide, ondansetron, droperidol, and promethazine. Of these antiemetics, droperidol and

promethazine are known to cause sedation. This may have interfered with the subject's perception of pain and the ability to provide accurate responses to the sensory and motor function tool. While the investigators did not notice any interference with data collection in the two subjects who received either droperidol or promethazine, the use of these drugs may have affected the results of this study. In one case, the nausea was most probably a side effect of morphine administered for postoperative pain in the PACU. It was noted that metoclopramide was administered 40 minutes after the administration of intravenous morphine for postoperative pain. There was no clearly defined causative factor for the nausea experienced by the subjects who received droperidol, promethazine, or ondansetron.

Lastly, the investigators were not able to standardize take home postoperative analgesics due to surgeon preference. Data were only collected via the telephone survey on subjects who did not experience pain in the hospital. The data collected could not be statistically analyzed because of the inability to convert the dosages of the analgesics administered into equivalent potencies.

Conclusions

Several conclusions can be derived from this study. The first conclusion made by the investigators was that the addition of morphine to a mepivacaine and epinephrine solution administered to the brachial plexus might delay the onset of postoperative surgical pain. This conclusion was supported by the greater delay in the onset of pain demonstrated by the axillary experimental group when compared to the axillary control group. In addition, the investigators concluded that for interscalene brachial plexus blocks, the ulnar nerve would have sensory and motor function return prior to other nerve fields. Axillary brachial plexus blocks have a different pattern for the return of sensory

and motor function. The axillary nerve will return first followed by the medial antebrachial cutaneous and musculocutaneous nerves.

The final conclusions made by the investigators are that patients having procedures of the hand, forearm, arm, and/or shoulder for which brachial plexus anesthesia is appropriate will experience a moderated level of postoperative pain. This pain will range from 4 to 6 on the numeric rating scale and can be treated with a variety of pain medications.

Implications for Nursing Anesthesia Practice

The findings of this study do not support the use of 75 mcg/kg morphine in the brachial plexus block solution to clinically delay the onset of postoperative pain. Additionally, the anesthesia care provider can expect sensory and motor functions to return in a predictable pattern following brachial plexus anesthesia. Finally, the anesthesia care provider can expect patients receiving brachial plexus anesthesia for surgeries of the hand, forearm, arm, and/or shoulder to experience a moderate level of postoperative pain. This pain can be controlled adequately with standard pain medications such as Percocet, Lortab, and Motrin.

Recommendations for Further Research

Although the results of this study are equivocal, future studies comparing brachial plexus anesthesia with and without the use of opioids in the local anesthetic solution are warranted with the following recommendations: First, the sample size must be large enough to have the power to detect relationships between variables. Next, the data collection tool on sensory and motor functions must be designed to detect the exact time of return of these functions. In addition, the use of supplemental blocks by the surgeon

APPENDIX A

Brachial Plexus Block Data Tool

To be completed by ACP

Brachial Plexus Block Data Tool

Instructions: Please complete this form on all study subjects and return form to the study file at the Operating Room. Thank You!

General Information

A. Subject # _____ B. Date of Surgery_____

C. Baseline pain: Location_____; Intensity (0-10)_____; Duration_____

Description (in patient's own words)_____

Patient Information

A. Name_____ B. Age_____ C. Sex: M F

D. Ethnicity: Black/Non-Hispanic ___ Hispanic ___ White/NonHispanic ___ Other_____

E. Telephone number (w/ area code) _____ F. ASA I II III IV E

_____

Surgical Information

A. Procedure_____

B. Length of Procedure (min.) _____ C. Tourniquet: Yes _____min. _____mmHg No

Brachial Plexus Block Information

A. Approach: Interscalene Axillary Interscalene/GETA B. Time injection ends_____

C. Number of Attempts: _____ D. Technique: Peripheral Nerve Stimulator Transarterial Paresthesia

E. Amount of local anesthetic injected into sheath_____ F. Ring Block Performed: Yes (cc's ____) No

G. Local Anesthetic Deposited in Coracobrachialis: Yes (cc's ____) No

H. Complete Block Partial Block Failed Block

I. Supplemental Block Required: Yes No Location: _____

J. Additional anesthetics/analgesics (including dose/route/time) administered during surgical procedure:

K. Remarks/Unusual Occurrences:

L. Arrival To PACU:_____(time)

(Please document motor and sensory on attached sheet)

Pain: Time of onset:_____; Location:_____; Intensity (0-10)_____

Description(in patient's own words)_____

Pain medications given:_____

1/2 in. left margin on all pages - necessary for binding

APPENDIX B

Sensory and Motor Assessment Tool

Sensory & Motor Assessment Tool

Sensory Innervation Assessment
(application of 18-gauge needle or sharp plastic applicator)

NERVE		REGION
Axillary	→	lateral side of arm
Musculocutaneous	→	lateral side of forearm
Radial	→	dorsum of hand over index finger's metacarpophalangeal joint
Median	→	thenar eminence
Ulnar	→	little finger
Medial cutaneous nerve of arm	→	medial side of the upper arm
Medial cutaneous nerve of forearm	→	medial side of the forearm

* Response will be documented using a 0 to 2 numeric rating scale:

0 = no loss of sensation to pinprick
1 = analgesia (patient feels touch but no pinprick)
2 = no sensation of touch

Motor Innervation Assessment
(Gravity and/or applied resistance)

NERVE		FUNCTION
Axillary	→	ability to abduct shoulder
Musculocutaneous	→	ability to flex the forearm
Radial	→	ability to extend the forearm
Median	→	ability to oppose the thumb and fifth finger
Ulnar	→	ability to adduct the little finger

* Response will be documented using a 0 to 2 numeric rating scale:

0 = no weakness
1 = paresis
2 = paralysis

APPENDIX C

Telephone Survey Tool

Telephone Survey Tool

Please write down the date and time of day you first:

1. Had feeling at the site of your surgery_____ am/pm
(This means if someone or something touched your arm, you could feel it.)

2. Were able to wiggle your fingers _____ am/pm
(On the same arm as your surgery)

3. Had pain at the site of your surgery_____ am/pm

a. Rate your pain on a scale from 0-10 (0 = no pain, 10 = the worst pain you have ever had). My pain is number _____.

b. Where on your body is your pain? Location_____.

c. Describe your pain_____.

4. What medicines have you taken?

Name of medicine_____

Amount_____

Time_____

Name of medicine_____

Amount_____

Time_____

Remember- someone will call you between 9 am and 11 am the day after your surgery to collect this information. Thank You!

APPENDIX D

Telephone Survey Teaching Tool

Telephone Survey Teaching Tool

(Instructions for investigator: Please read this script verbatim to all study subjects. Fill in data requested at the bottom of this sheet. Give the Telephone Survey Tool to the subject. Return this form to the subject's folder)

Mr./Mrs._____, someone will be calling you tomorrow between 9 and 11 AM to ask some questions about how you're doing after the surgery. Specifically they will want the answers to these questions. (give card to subject). Please fill this card out as precisely as you can. The exact times are very important to the success of study.

The first question is about the time you first had feeling at the site of your surgery. This means if someone or something touched you, you could feel it.

The second question is about the first time you could wiggle your fingers on the same arm as your surgery. (demonstrate)

The third question is about the first time you had pain at the site of your surgery. Please write this time down *before* you take medicine for the pain. Related to this pain we will also need to know the following:

Rated on a scale from 0 to 10 with 0 equaling no pain and 10 equaling the worst pain that you have ever experienced, what is your pain score? Where on your body was the pain?

And, would you please describe this pain? (burning, throbbing, aching, sharp, dull, etc)

You will also be asked what medicines you have taken for pain. This will include the type, amount and time. We only need to know this information for the first time that you took the pain medicine.

The accuracy of these times is very important to the success of this study and your help is greatly appreciated. Please remember that we will be calling you tomorrow between 9 and 11 AM. If you anticipate not being home, is there another phone number at which we can reach you? If you have completed the data on the survey tool and will not be available at these times, someone else may provide us with the information on the tool.

CONFIRM HOME PHONE NUMBER:_____

OTHER NUMBER:_____

Do you have any questions?

APPENDIX E

Prepared Telephone Script

Investigators Telephone Script

Hello Mrs/Mr._____. This is

_____ with the anesthesia department

at_____. I am calling to collect the information from the card you were given. Is now a good time for you to talk? (If not, obtain a time to call back.)

Do you have your card in front of you? (If not suggest that subject get card so as to provide exact information).

Tell me the first time you had feeling at the site of your

surgery_____

Tell me the first time you were able to wiggle your

fingers_____

Tell me the time you first had pain at your surgical

site_____

Have you taken any pain medications since you got home?

Type_____ Reason for taking the Medication_____

Time_____

Amount_____

Have you experienced any of the following: (circle all that apply)

Itching

Nausea

Vomiting

Drowsiness

Other information provided by subject (describe)

APPENDIX F

PACU/ASC/Ward Data Collection Worksheet

PACU /ASC/WARD DATA COLLECTION WORKSHEET

PACU (INTRA)

Onset of pain (time)_____ Intensity Scale (0 – 10)____ Site of Pain_____ Description of Pain_____
Respiratory Rate_____ If < 8 breaths per minute, room air SaO2_____

Medications Given:	Time	Dose		Time	Dose
MSO4			Narcan		
Toradol			Zofran		
Demerol			Benadryl		
Other_____			Droperidol		
			Other_____		

(Please circle or List)
Side Effects: Nausea Vomiting Pruritis Urinary Retention
Other_____

SRNA ASSESSMENT ***Motor 0 1 2*** ***Sensory 0 1 2***

PACU (DISCHARGE)

Onset of pain (time)_____ Intensity Scale (0 – 10)____ Site of Pain_____ Description of Pain_____
Respiratory Rate_____ If < 8 breaths per minute, room air SaO2_____

Medications Given:	Time	Dose		Time	Dose
MSO4			Narcan		
Toradol			Zofran		
Demerol			Benadryl		
Other_____			Droperidol		
			Other_____		

(Please circle or List)
Side Effects: Nausea Vomiting Pruritis Urinary Retention
Other_____

SRNA ASSESSMENT ***Motor 0 1 2*** ***Sensory 0 1 2***

ASC (INTRA)

Onset of pain (time)_____ Intensity Scale (0 – 10)____ Site of Pain_____ Description of Pain_____
Respiratory Rate_____ If < 8 breaths per minute, room air SaO2_____

Medications Given:	Time	Dose		Time	Dose
MSO4			Narcan		
Toradol			Zofran		
Demerol			Benadryl		
Other_____			Droperidol		
			Other_____		

(Please circle or List)
Side Effects: Nausea Vomiting Pruritis Urinary Retention
Other_____

SRNA ASSESSMENT ***Motor 0 1 2*** ***Sensory 0 1 2***

ASC (DISCHARGE)

Onset of pain (time)_____ Intensity Scale (0 – 10)____ Site of Pain_____ Description of Pain_____
Respiratory Rate_____ If < 8 breaths per minute, room air SaO2_____

Medications Given:	Time	Dose		Time	Dose
MSO4			Narcan		
Toradol			Zofran		
Demerol			Benadryl		
Other_____			Droperidol		
			Other_____		

(Please circle or List)
Side Effects: Nausea Vomiting Pruritis Urinary Retention
Other_____

TELEPHONE/VISIT SURVEY
Onset of Pain_____ Intensity (0 – 10)_____ Site_____ Description_____ Return of Motor_____ Return of Sensory_____
Meds_____
Side Effects_____

APPENDIX G

Informed Consent

Reference List

Aanta, R., Kirvela, O., Lahdenpera, A., & Nieminen, S. (1994). Transarterial brachial plexus anesthesia for hand surgery: A retrospective analysis of 346 cases. Journal of Clinical Anesthesia, 6, 189-192.

Armstrong, P., Power, J., & Wildsmith, J. A. (1991). Addition of fentanyl to prilocaine for intravenous regional anaesthesia. Anaesthesia, 46, 278-280.

Attolini, L., Gantenbein, M., Grignon, S., & Bruguerolle, B. (1995). Effects of clonidine pretreatment on the local anesthetic activity of bupivacaine in mice. Journal of Pharmacy and Pharmacology, 47, 994-996.

Bates, M., Edwards, W., & Anderson, K. (1993). Ethnocultural influences on variation in chronic pain perception. Pain, 52, 101-112.

Bazin, J., Massoni, C., Bruelle, P., Fenies, V., Groslier, D., & Schoeffler, P. (1997). The addition of opioids to local anaesthetics in brachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia, 52, 858-862.

Bedder, M. D., Kozody, R., & Craig, D. B. (1988). Comparison of bupivacaine and alkalinized bupivacaine in brachial plexus anesthesia. Anesthesia and Analgesia, 67, 48-52.

Benet, L. Z. (1996). Introduction. In J. G. Hardman, L. E. Limbird, P. B. Molinoff, R. W. Ruddon, & A.G. Gilman (Eds.), Goodman & Gilman's the parmacological basis of therapeutics (9th ed., p. 1). New York: McGraw-Hill.

Bernard, J. M., & Macaire, P. (1997). Dose-range effects of clonidine added to lidocaine for brachial plexus block. Anesthesiology, 87, 277-284.

Berne, R. M., & Levy, M. N. (1996). Preface. In R. M. Berne & M. N. Levy (Eds.), Principles of physiology (2nd ed., p. vii). St. Louis: Mosby.

Bloomstone, J., & Borsook, D. (1998). Pain. In W. E. Huford, M. T Bailin, J. K. Davison, K. L. Haspel, & C Rosow (Eds.), Clinical anesthesia procedures of the Massachusetts general hospital (5th ed., pp. 661-667). Philadelphia: Lippincott.

Bonica, J. J. (1990). In J. J. Bonica (Ed.), The management of pain (2nd ed., pp.19-20, 180-189). Philadelphia: Lea & Febiger.

Bourke, D. L., & Furman, W. R. (1993). Improved postoperative analgesia with morphine added to axillary block solution. Journal of Clinical Anesthesia, 5, 114-117.

Bozkurt, P., Kaya, F., & Yeker, Y. (1997). Single-injection lumbar epidural morphine for postoperative analgesia in children: A report of 175 cases. Regional Anesthesia, 22 (3), 212-217.

Bridenbaugh, L. D. (1988). The upper extremity: Somatic blockade. In M. J. Cousins & P. O. Bridenbaugh (Eds.), Neural blockade in clinical anesthesia and management of pain (2nd ed., pp. 387-416). Philadelphia: Lippincott.

Brody, G. A. & Egan, T. D. (1996). Hand surgery. In R. A. Jaffe & S. I. Samuels (Eds.), Anesthesiologist's manual of surgical procedures (pp. 585-597). Philadelphia: Lippincott.

Bromage, P. R. (1976). Mechanism of action. In P. R. Bromage (Ed.), Epidural analgesia (pp. 119-159). Philadelphia: W. B. Saunders.

Brown, D. L. (1994). Brachial plexus anesthesia: An analysis of options. Yale Journal of Biology and Medicine, 66, 415-431.

Brown, R. S., Redden, R. J., & Chan, J. T. (1995). The evaluation of a reported allergic reaction to an amide local anesthetic: A case report. Texas Dental Journal, 112 (3), 37-40.

Carpenter, R. L., & Mackey, D. C. (1997). Local anesthetics. In P.G.Barash, B. F. Cullen, & R. K. Stoelting (Eds.), Clinical anesthesia (3rd ed., pp. 413-438). Philadelphia: Lippincott.

Catterral, W. A., & Mackie, K. (1996). Local Anesthetics. In J. G. Hardman, L. E. Limbird, P. B. Molinoff, R. W. Ruddon, & A. G. Gilman (Eds.), Goodman & Gilman's the pharmacological basis of therapeutics (9th ed., pp. 331-348). New York: McGraw-Hill.

Cave, L. A. (1989). Follow-up phone calls after discharge. American Journal of Nursing, 942-943.

Coda, B. A. (1997). Opioids. In P.G.Barash, B. F. Cullen, & R. K. Stoelting (Eds.), Clinical anesthesia (3rd ed., pp. 329-358). Philadelphia: Lippincott.

Cohen, J. (1992). A power primer. Psychological Bulletin, 112 (1), 155-159.

Cousins, M. J., Cherry, D.A., & Gourlay, G. K. (1988). Acute and chronic pain: Use of spinal opioids. In M. J. Cousins & P. O. Bridenbaugh (Eds.), Neural blockade in clinical anesthesia and management of pain (2nd ed., pp. 955-1030). Philadelphia: Lippincott.

Cousins, M. J., & Mather, L. E. (1984). Intrathecal and epidural administration of opioids. Anesthesiology, 61, 276-310.

Davis, P. (1993). Opening up the gate control theory. Nursing Standard, 7 (45), 25-27.

de Jong, R. H. (1996). Local anesthetic pharmacology. In D. L. Brown (Ed.), Regional anesthesia and analgesia (pp. 124- 142). Philadelphia: W.B. Saunders.

Dennison, A., Oakley, N., Appleton, D., Paraskevopoulos, J., Kerrigan, D., Cole, J., & Thomas, W. E. G. (1995). Local anaesthesia for major general surgical procedures: A review of 116 cases over 12 years. Postgraduate Medical Journal, 72, (844), 105-108.

DePalma, M., & Weisse, C. (1997). Psychological influences on pain perception and non-pharmacologic approaches to the treatment of pain. Journal of Hand Therapy, 2, 183-189.

Dhawan, B. N., Cesselin, F., Raghubir, R., Reisine, T., Bradley, P. B., Portoghese, P. S., & Hamon, M. (1996). International union of pharmacology: Classification of opioid receptors. Pharmacological Reviews, 48 (4), 567-592.

Donnelly, A. J., Cunningham, F. E., & Baughman, V. L. (1999). Anesthesiology and critical care drug handbook (2nd ed.). Cleveland: Lexi.

Dorman, B. H., Conroy, J. M., Duc, T. A., Haynes, G. R., & Friedman, R. J. (1994). Postoperative analgesia after major shoulder surgery with interscalene brachial plexus blockade: Etidocaine versus bupivacaine. Southern Medical Journal, 87 (4), 502-505.

Duncan, G., Bushnell, M., & Lavigne, G. (1989). Comparison of verbal and visual analogue scales for measuring the intensity and unpleasantness of experimental pain. Pain, 37, 295-303.

Edwards, R., Abullarade, C., & Turnbull, N. (1996). Nursing management and follow-up of the postoperative vascular patient in a clinical setting. Journal of Vascular Nursing, XIV (3), 62-67.

Flaherty, S. A. (1996). Pain measurement tools for clinical practice and research. Journal of the American Association of Nurse Ansthetists, 64 (2), 133-140.

Fletcher, D., Kuhlman, G., & Samii, K. (1994). Addition of fentanyl to 1.5% lidocaine does not increase the success of axillary plexus block. Regional Anesthesia, 19 (3), 183-188.

Flory, N., Van-Gessel, E., Donald, F., Hoffmeyer, P. ,& Gamulin, Z. (1995). Does the addition of morphine to brachial plexus block improve analgesia after shoulder surgery? British Journal of Anaesthesia, 75, 23-26.

Freysz, M., Timour, Q., Bertrix, L., Loufoua, J., Aupetit, J., & Faucon, G. (1995). Bupivacaine hastens the ischemia-induced decrease of the electrical ventricular fibrillation threshold. Anesthesia and Analgesia, 80, 657-663.

Friedman, H. E., Jules, K. T., Springer, K., & Jennings, M. (1997). Buffered lidocaine decreases the pain of digital anesthesia in the foot. Journal of the American Podiatric Medical Association, 87 (5), 219-223.

Fujimura, N., Namba, H., Tsunoda, K., Kawamata, T., Taki, K., Igarasi, M., & Namiki, A. (1995). Effect of hemidiaphragmatic paresis caused by interscalene brachial plexus block on breathing pattern, chest wall mechanics, and arterial blood gases. Anesthesia and Analgesia, 81, 962-966.

Gantenbein, M., Attolini, L., & Bruguerolle. B. (1996). Potassium channel agonists modify the local anesthetic activity of bupivacaine in mice. Canadian Journal of Anaesthesia, 43 (8), 871-876.

Gissen, A. J., Gugino, L. D., Datta, S., Miller, J., & Covino, B. G. (1987). Effects of fentanyl and sufentanil on peripheral mammalian nerves. Anesthesia and Analgesia, 66, 1272-1276.

Gormley, W. P., Hill, D. A., Murray, J. M.,& Fee, J. P. (1996). The effect of alkalinization of lignocaine on axillary brachial plexus anesthesia. Anaesthesia, 51 (2), 185-188.

Greenblatt, G., & Denson, J. (1962). Needle nerve stimulator locator: Nerve block with a new instrument for locating nerves. Anesthesia and Analgesia, 41 (5), 599-602.

Harkins, S. W., Kwentus, J., & Price, D. D. (1990). In J. J.Bonica (Ed.), The management of pain (2nd ed., pp. 552-559). Philadelphia: Lea & Febiger.

Hensyl, W. R. (Ed.). (1990). Stedman's medical dictionary (25th ed., p.65). Baltimore: Williams & Wilkins.

Hickey, R., Hoffman, J., & Ramamurthy, S. (1991). A comparison of ropivacaine 0.5% and bupivacaine 0.5% for brachial plexus block. Anesthesiology, 74, 639-642.

Hickey, R., Rogers, J. N., Hoffman, J., Ramamurthy, S., & Tingle L. J. (1993). Comparison of the clinical efficacy of three perivascular techniques for axillary brachial plexus block. Regional Anesthesia, 18, 335-338.

Hickey, R., Rowley, C. L., Candido, K. D., Hoffman, J., Ramamurthy, S., & Winnie, A. P. (1992). A comparative study of 0.25% ropivacaine and 0.25% bupivacaine for brachial plexus block. Anesthesia and Analgesia, 75, 602-606.

Horlocker, T. T. (1996). Concurrent medical problems and regional anesthesia. In D. L. Brown (Ed.), Regional anesthesia and analgesia (pp. 423-445). Philadelphia: W. B. Saunders.

Jones, T. S. (1997). Comparison of axillary block techniques: Is there a difference in success rates? Journal of the American Association of Nurse Anesthetists, 65, 257-259.

Joris, J. L., Dubner, R., & Hargreaves, K. M. (1987). Opioid analgesia at peripheral sites: a target for opioids released during stress and inflammation? Anesthesia and Analgesia, 66, 1277-1281.

Kardash, K., Schools, A., & Concepcion, M. (1995). Effects of brachial plexus fentanyl on supraclavicular block. Regional Anesthesia, 20 (4), 311-315.

Kehlet, H., & Dahl, J. (1993). The value of 'multimodal" or "balanced anesthesia" in postoperative pain treatment. Anesthesia and Analgesia, 77, 1048-1056.Koscielniak-Nielsen, Z. J., Christensen, L., Stens- Pedersen, H. L., & Brushoj, J. (1995). Effect of digital pressure on the neurovascular sheath during perivascular axillary block. British Journal of Anaesthesia, 75, 702-706.Koscielniak-Nielsen, Z. J., Stens-Pedersen, H. L., & Lippert, F. K. (1997). Readiness for surgery after axillary block: Single or multiple injection techniques. European Journal of Anaesthesiology, 14, 164-171.

Lan, C., Wen, C., Tan, C., Ling, E., & Shieh, J. (1995). A comparative ultrastructural study of primary afferents from the brachial and cervical plexuses to the external cuneate nucleus of gerbils. Journal of Anatomy, 187, 115-125.

Langerman, L., Bansinath, M., & Grant, G. J. (1994). The partition coefficient as a predictor of local anesthetic potency for spinal anesthesia: Evaluation of five local anesthetics in a mouse model. Anesthesia and Analgesia, 79, 490-494.

Lipton, J. A., & Marbach, J. (1984). Ethnicity and the pain experience. Social Science Medicine, 84, 1279-1298.

Liu, S., Carpenter, R. L., Chiu, A. A., McGill, T. J., & Mantell, S. A. (1995). Epinephrine prolongs duration of subcutaneous infiltration of local anesthesia in a dose-related manner. Regional Anesthesia, 20 (5), 378-384.

Mackay, C. A., & Bowden, D. F. (1997). Axillary brachial plexus block: An underused technique in the accident and emergency department. Journal Accident and Emergency Medicine, 14, 226-229.

Mancuso, C. A., & Charlson, M. E. (1995). Does recollection error threaten the validity of cross-sectional studies of effectiveness? Medical Care, 33 (4), 77-88.

Marcus, A. C., & Crane, L. A. (1986). Telephone surveys in public health research. Medical Care, 24 (2), 97-112.

Mays, K., Lipman, J., & Schnapp, M. (1987). Local analgesia without anesthesia using peripheral perineural morphine injections. Anesthesia and Analgesia, 66, 417-420.

McGuire, D. (1983). The measurement of clinical pain. Nursing Research, 33 (3), 152-158.

Minami, M., & Satoh, M. (1995). Molecular biology of the opioid receptors: Structures, functions and distributions. Neuroscience Research, 23, 121-145.

Moller, R. A., & Covino, B. G. (1993). Cardiac electrophysiologic effects of articaine compared with bupivacaine and lidocaine. Anesthesia and Analgesia, 76, 1266-1273.

Mulroy, M. F. (1997). Peripheral nerve blockade. In P. Barash, B. F. Cullen, & R. K. Stoelting (Eds.), Clinical anesthesia (3rd ed., pp. 669-698). Philadelphia: Lippincott.

Nail, L. M., Greene, D., Jones, L. S., & Flannery, M. (1989). Nursing care by telephone: Describing practice in an ambulatory oncology center. Oncology Nursing Forum, 16 (3), 387-395.

Norman, G. R. & Streiner, D. L. (1999). PDQ stats (2nd ed.,p. 47). St. Louis: B. C. Decker.

Omoigui, S. (1995). The anesthesia drugs handbook (2nd ed., pp. 199-202). St. Louis: Mosby.

Partridge, B. L., Katz, J., & Benirschke, K. (1987). Functional anatomy of the brachial plexus sheath: Implications for anesthesia. Anesthesiology, 66, 743-747.

Passannante, A. N. (1996). Spinal anesthesia and permanent neurologic deficit after interscalene block. Anesthesia and Analgesia, 82, 873-874.

Pasternak, G. W. (1993). Pharmacological mechanisms of opioid analgesics. Clinical Neuropharmacology, 16 (1), 1-18.

Pippa, P., Aito, S., Cominelli, E., Doni, L., Rabassini, M., Marinelli, C., & Micozzi, S. (1992). Brachial plexus block using the transcoracobrachial approach. European Journal of Anaesthesiology, 9, 235-239.

Polit, D., & Hungler, B. (1995). Nursing research principles and methods. Philadelphia: Lippincott.

Quinlan, J., Oleksey, K., & Murphy, F. (1992). Alkalinization of mepivacaine for axillary block. Anesthesia and Analgesia, 74, 371-374.

Racz, H., Gunning, K., Della Santa, D., & Forster, A. (1991). Evaluation of the effect of perineuronal morphine on the quality of postoperative analgesia after axillary plexus block: a randomized double-blind study. Anesthesia and Analgesia, 72, 769-772.

Raftery, K., Smith-Coggins, R., & Chen, A. (1995). Gender- associated differences in emergency department pain management. Annals of Emergency Medicine, 26 (4), 414-421.

Ransom, D. M. & Leicht, C. H. (1996). Postdelivery analgesia. In D. L. Brown (Ed.), Regional anesthesia and analgesia (pp. 625-631). Philadelphia: W. B. Saunders.

Ready, L. B. (1994). Acute postoperative pain. In R. D. Miller (Ed.), Anesthesia (4th ed., pp. 2327-2341). New York: Churchill Livingstone.

Reisine, T. & Pasternak, G.W., (1996). Opioid analgesics and antagonists. In J. G. Hardman, L. E. Limbird, P. B. Molinoff, R. W. Ruddon, A. G. Gilman (Eds.), Goodman & Gilman's the pharmacological basis of therapeutics (9th ed., p.p. 521-553). New York: McGraw-Hill.

Rucci, F., Pippa, P., Boccaccini, A., & Barbagli, R. (1995). Effect of injection speed on anaesthetic spread during axillary block using the orthogonal two-needle technique. European Journal of Anaesthesiology, 12, 505-511.

Sanchez R., Nielson H., Heslet L., & Iverson A. D. (1984). Neuronal blockade with morphine. A hypothesis. Anaesthesia, 39 (8), 788-789.

Santos, A. C., Arthur, G. R., Wlody, D., De Armas, P., Morishima, H. O. & Finster, M. (1995). Comparative systemic toxicity of ropivacaine and bupivacaine in nonpregnant and pregnant ewes. Anesthesiology, 82 (3), 734-740.

Schroeder, L. E., Horlocker, T. T., & Schroeder, D. R. (1996). The efficacy of axillary block for surgical procedures about the elbow. Anesthesia and Analgesia, 83, 747-751.

Scott, I. E. (1992). Nurses' attitudes to pain control and the use of pain assessment scales. British Journal of Nursing, 2 (1), 111-116.

Scott, I. E. (1994). Effectiveness of documented assessment of postoperative pain. British Journal of Nursing, 3 (10), 494-501.

Sisk, A. L., Grover, B., & Steflik, D. E., (1991). Long-term memory of acute post surgical pain. Journal of oral and maxillofacial surgery, 49, 353-358.

Skidmore, R. A., Patterson, J. D., & Tomsick, R. S., (1996). Local anesthetics. Dermatological Surgery, 22, 511-522.

Stan, T. C., Krantz, M. A., Solomon, D. L., Poulos, J. G., & Chaouki, K. (1993). The incidence of neurovascular complications following axillary brachial plexus block using a transarterial approach: A prospective study of 1,000 consecutive patients. Regional Anesthesia, 20 (6), 486-492.

Stein, C. (1993). Peripheral mechanisms of opioid analgesia. Anesthesia and Analgesia, 76, 182-191.

Stein, C. (1995). The control of pain in peripheral tissue by opioids. The New England Journal of Medicine, 332, 1685-1690.

Stein, C., Millan, M. J., Shippenberg, T. S., Peter, K., & Herz, A. (1988). Peripheral opioid receptors mediating antinociception in inflammation. Evidence for involvement of mu, delta, and kappa receptors. The Journal of Pharmacology and Experimental Therapeutics, 248 (3), 1269-1275.

Stoelting, R. (1995). Handbook of pharmacology and physiology in anesthetic practice (pp. 123-144). Philadelphia: Lippincott.

Sukhani, R., Barclay, J. & Aasen, M. (1994). Prolonged Horner's syndrome after interscalene block: A management dilemma. Anesthesia and Analgesia, 79, 601-603.

Tetzlaff, J., Yoon, H., & Brems, J. (1993). Patient acceptance of interscalene block for shoulder surgery. Regional Anesthesia, 18, 30-33.

Tetzlaff, J., Yoon, H., Brems, J., & Javorsky, T. (1995). Alkalinization of mepivacaine improves the quality of motor block associated with interscalene brachial plexus anesthesia for shoulder surgery. Regional Anesthesia, 20 (2), 128-132.

Tetzlaff, J., Yoon, H., O'Hara, J., Reaney, J., Stein, D., & Grimes-Rice, M. (1990). Alkalinization of mepivacaine accelerates onset of interscalene block for shoulder surgery. Regional Anesthesia, 15, 242-244.

Thomas, C. (Ed.). (1993). Taber's encylopedic medical dictionary (17th ed., p. 1914). Philidelphia: F. A. Davis.

Thompson, G. E., & Rorie, D. K. (1983). Functional anatomy of the brachial plexus sheaths. Anesthesiology, 59, 117-122.

Thorpe, D. H. (1984). Opiate structure and activity- a guide to understanding the receptor. Anesthesia and Analgesia, 63, 143-151.

Tulchinsky, A., Weller, R., Rosenblum, M., & Gross, J. (1993). Nerve stimulator polarity and brachial plexus block. Anesthesia and Analgesia, 77, 100-103.

Urban, M., & Urquhart, B. (1994). Evaluation of brachial plexus anesthesia for upper extremity surgery. Regional Anesthesia, 19 (3), 175-182.

Urmey, W. F. (1996). Upper Extremity Blocks. In D. L. Brown (Ed.), Regional anesthesia and analgesia (pp. 254-278). Philadelphia: W. B. Saunders.

Urmey, W. F. & McDonald, M. (1992). Hemidiaphragmatic paresis during interscalene brachial plexus block: Effects on pulmonary function and chest wall mechanics. Anesthesia and Analgesia, 74, 352-357.

Veering, B. T. (1996). Local anesthetics. In D. L. Brown (Ed.), Regional anesthesia and analgesia (pp. 188-207). Philadelphia: W. B. Saunders.

Viel, E. J., Eledjam, J. J., De La Coussaye, J. E., & D'athis, F. (1989). Brachial plexus block with opioid for postoperative pain relief: Comparison between buprenorphine and morphine. Regional Anesthesia, 14 (6), 274-278.

Wedel, D. J., Horlocker, T. T. (1997). Anesthesia for orthopaedic surgery. In P. G. Barash, B. F. Cullen, & R. K. Stoelting, (Eds.). Clinical anesthesia (3rd ed., pp. 1025-1038). Philadelphia: Lippincott.

Winnie, A. P. (1990). Plexus anesthesia: Vol.1. Perivascular techniques of brachial plexus block. (pp. 121-144).Philadelphia: W. B. Saunders.

Winnie, A. P. (1995). Does the transarterial technique of axillary block provide a higher success rate and lower complication rate than a paresthesia technique? Regional Anesthesia, 20 (6), 482-485.

Worth, A., & Tierney, A. J. (1993). Conducting research interviews with elderly people by telephone. Journal of Advanced Nursing, 18, 1077-1084.

Yamamoto, K., Tsubokawa, T., Shibata, K., & Kobayashi, T. (1995). Area of paresthesia as determinant of sensory block in axillary brachial plexus block. Regional Anesthesia, 20 (6), 493-497.

Young, W. S., Wamsley, J. K., Zarbin, M. A., & Kuhar, M. J. (1980). Opioid receptors undergo axonal flow. Science, 210 (3), 76-77.